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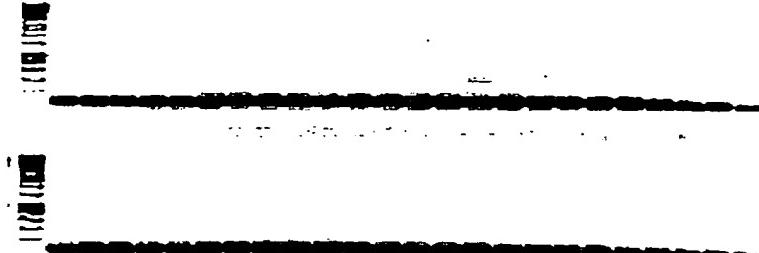
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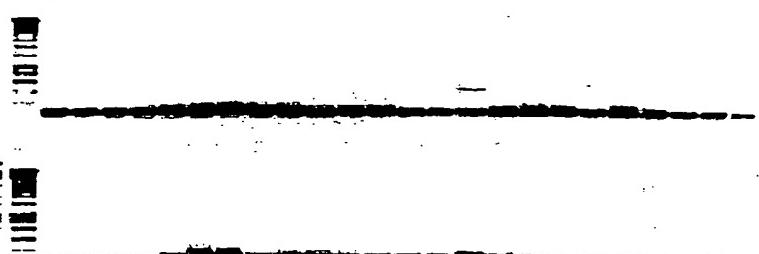
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(54) Title: TISSUE SPECIFIC GENES AND GENE CLUSTERS

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pancreatic function. A cluster of transmembrane and GPCR-type receptor genes is also located at chromosomal band 11q12.2. These genes are expressed predominantly in the spleen (hence, "spleen gene" cluster), as well as other tissues of the immune and reticuloendothelial system (RES), indicating that establishing this region of the chromosome is involved in spleen, lymphoid, and/or reticuloendothelial function. Finally, genes coding for membrane proteins have been identified which are expressed selectively in bone marrow, kidney, pancreas, and retina.

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TISSUE SPECIFIC GENES AND GENE CLUSTERS

This application claims the benefit of U.S. Application Serial Nos. 60/372,669 April 16, 2002, 60/374,823 filed April 24, 2002, 60/376,558 filed May 1, 2002, 60/381,366 filed 5 May 20, 2002, 60/403,648 filed August 16, 2002, 60/411,882 filed September 20, 2002, and 60/424,336 filed November 7, 2002, which are hereby incorporated by reference in their entirety.

DESCRIPTION OF THE DRAWINGS

Figs. 1 and 2 show a physical map of the immune system gene complex. Sequence-tagged site ("STS") markers are used to characterize the chromosomal regions. An STS is defined by two short synthetic sequences (typically 20 to 25 bases each) that have been designed from a region of sequence that appears as a single-copy in the human genome (the reference numbers, and the sequences which they represent, are hereby incorporated by reference in their entirety). These sequences can be used as primers in a polymerase chain reaction (PCR) assay to determine whether the site is present or absent from a DNA sample.

Fig. 3 shows the expression pattern of transmembrane proteins homologous to the olfactory G-protein-coupled receptor ("GPCR") family in human tissues. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 5 indicates the SEQ ID NO for each primer ("FOR" is the forward primer and "REV" is the reverse primer).

Fig. 4 shows the expression pattern of two olfactory G-protein-coupled receptor ("GPCR") family members in human tissues. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 6 indicates the SEQ ID NO for each primer ("FOR" is the forward primer and "REV" is the reverse primer).

Figs. 5 (a and b) and 6 show the expression pattern in human tissues of genes selectively expressed in kidney tissue. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 11 indicates the SEQ ID NO for each primer ("FOR" is the forward primer and "REV" 30 is the reverse primer).

Fig. 7 (a-b) show organization of pancreatic gene complex on chromosome 11q24.

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Fig. 8 is a schematic drawing of five of the pancreatic olfactory G-protein-coupled receptor ("GPCR") family members located in the gene complex showing regions of overlap. The numbering underneath the lines indicates amino acid position.

Fig. 9 (a and b) show the expression pattern of TMD0986, XM_061780 (TMD0987),
5 XM_061781 (TMD0353), XM_061784 (TMD0989), and XM_061785 (TMD058) in human tissues. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 12 indicates the SEQ ID NO for each primer ("FOR" is the forward primer and "REV" is the reverse primer).

Fig. 10 shows the expression pattern of TMD1030 (XM_166853), TMD1029
10 (XM_166854), TMD1028 (XM_166855), and TMD0621 (XM_166205) in human tissues. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 17 indicates the SEQ ID NO for each primer ("F-oligo" is the forward primer and "R-oligo" is the reverse primer).

Fig. 11 shows the organization of the spleen gene complex on chromosome 11q12.2.

15 Fig. 12 (a-c) shows the expression of the pancreas genes in human tissues. To detect gene expression, PCR was carried out on aliquots of the normalized tissue samples using a forward and reverse gene-specific primers. Table 23 indicates the SEQ ID NO for each primer ("FOR" is the forward primer and "REV" is the reverse primer).

Expression patterns were analyzed as described below. A twenty-four tissue panel
20 was used (lanes from left to right): 1, adrenal gland; 2, bone marrow; 3, brain; 4, colon; 5, heart; 6, intestine; 7, pancreas; 8, liver; 9, lung; 10, lymph node; 11, lymphocytes; 12, mammary gland; 13, muscle; 14, ovary; 15, pancreas; 16, pituitary; 17, prostate; 18, skin; 19, spleen; 20, stomach; 21, testis; 22, thymus; 23, thyroid; 24, uterus. The lane at the far left of each panel contains molecular weight standards. Polyadenylated mRNA was isolated from
25 tissue samples, and used as a template for first-strand cDNA synthesis. The resulting cDNA samples were normalized using beta-actin as a standard. For the normalization procedure, PCR was performed on aliquots of the first-strand cDNA using beta-actin specific primers. The PCR products were visualized on an ethidium bromide stained agarose gel to estimate
30 the quantity of beta-actin cDNA present in each sample. Based on these estimates, each sample was diluted with buffer until each contained the same quantity of beta-actin cDNA per unit volume. PCR was carried out using the primers described above, and reaction

products were loaded on to an agarose (e.g., 1.5-2%) gel and separated electrophoretically.

DESCRIPTION OF THE INVENTION

The present invention relates to tissue-selective genes and tissue-selective gene clusters. The polynucleotides and polypeptides are useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting, diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, associated with genes of the present invention. The identification of specific genes, and groups of genes, expressed in pathways physiologically relevant to particular tissues, permits the definition of functional and disease pathways, and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clinical applications. The present invention also relates to methods of using the polynucleotides and related products (proteins, antibodies, etc.) in business and computer-related methods, e.g., advertising, displaying, offering, selling, etc., such products for sale, commercial use, licensing, etc.

Immune Gene Complex

The present invention relates to a group of genes involved in the function and activity of the immune system. These genes are organized into a discrete cluster at chromosomal location 1q22 (the "immune gene complex") and span hundreds of kb of DNA, e.g., about 700 kb of DNA. See, Figs. 1 and 2. The region closest to the centromere comprises genes that are expressed predominantly in the thymus, while the distal region comprises genes which are expressed predominantly in the bone marrow and other hematopoietic cells.

The present invention relates to a composition consisting essentially of the 1q22 immune gene complex, comprising TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) genes, or a fragment thereof comprising at least two said genes. As discussed in more detail, the composition can comprise or consist essentially of the chromosome region between STS markers that define the genomic DNA, e.g., between SHGC-81033 and SHGC-145403, or a fragment thereof comprising at least two said genes.

The CD1 family, a cluster of genes previously identified as coding for proteins involved in antigen presentation (Sugita and Brenner, Seminars in Immunology, 12:511-516, 2000), are located at the proximal boundary of the immune gene complex. The expression of CD1a, b, and c genes are restricted to professional antigen-presenting cells, including 5 dendritic cells and some B-cell subsets (Sugita and Brenner, *ibid*). CD1d is present on other cell types, in addition to hematopoietic cells, such as intestinal cells (Sugita and Brenner, *ibid*).

Adjacent to the CD1 family, is a cluster of genes coding for transmembrane proteins homologous to the olfactory G-protein-coupled receptor ("GPCR") family. These genes 10 include XM_060945 (TMD0024), XM_060346 (TMD1779), XM_060947 (TMD0884), and XM_060948 (TMD0025), and are expressed predominantly in thymus tissues (e.g., thymocytes). XM_089421 (TMD1781) is also expressed in thymus, but it is present in much higher amounts in lymphocytes ("PBL"). This chromosomal region can be defined by STS 15 markers, e.g., between SHGC-81033 and D1S3249, G15944, GDB:191077, GDB:196442, RH68459, RH102597, RH69635, or RH65132, or fragments thereof, such as fragments which comprise two or more genes.

The gene for human erythroid alpha spectrin (SPTA1) is distal to the GPCR thymus-restricted family. It is expressed in bone marrow cells, and is localized to the red cell membrane (Wilmotte et al., *Blood*, 90(10):4188-96, 1997). Next to it, is another cluster of 20 genes coding for proteins that resemble the olfactory GPCR family. These include XM_060956 (TMD0304), XM_060957 (TMD0888), and XM_060959 (TMD089), and are expressed predominantly in the bone marrow, although other sites of expression are observed as well. See, e.g., Table 1. This chromosomal region can be defined by STS markers, e.g., between GDB:181583 or RH118729, and D1S2577 or SHGC-145403.

25 The gene for myeloid cell nuclear differentiation antigen ("MNDA") is next. MNDA is also expressed in bone marrow cells, particularly in normal and neoplastic myelomonocytic cells and a subset of normal and neoplastic B lymphocytes (Miranda et al., *Hum. Pathol.*, 30(9):1040-9, 1999).

30 The phrase "immune system" indicates any processes and cells which are involved in generating and carrying out an immune response. Immune system cells includes, but are not limited to, e.g., stem cells, pluripotent stem cell, myeloid progenitor, lymphoid progenitor,

- lymphocytes, B-lymphocytes, T-lymphocytes (e.g., naive, effector, memory, cytotoxic, etc.), thymocytes, natural killer, erythroid, megakaryocyte, basophil, eosinophil, granulocyte-monocyte, accessory cells (e.g., cells that participate in initiating lymphocyte responses to antigens), antigen-presenting cells (“APC”), mononuclear phagocytes, dendritic cells, 5 macrophages, alveolar macrophages, etc., and any precursors, progenitors, or mature stages thereof.

Table I is a summary of the genes and their expression patterns in accordance with the present invention. The genes and the polypeptides they encode can be used as diagnostic, prognostic, therapeutic, and research tools for any conditions, diseases, disorders, or 10 applications associated with the tissues and cells in which they are expressed.

When expression is described as being “predominantly” in a given tissue, this indicates that the gene’s mRNAs levels are highest in this tissue as compared to the other tissues in which it was measured. Expression can also be “selective,” where expression is observed. By the phrase “selectively expressed,” it is meant that a nucleic acid molecule 15 comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, etc., or more) in that tissue when compared to other tissue-types.

In view of their selectivity and display on the cell surface, the olfactory GPCR family members of the present invention are a useful target for histological, diagnostic, and therapeutic applications relating to the cells in which they are expressed. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited to, imaging, 20 therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2 antibodies are used to breast cancer. They can also be used to detect metastatic cells, in biopsies to identify bone marrow and thymus tissue, etc. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to 25 target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc.

Useful antibodies or other binding partners include those that are specific for parts of the

polypeptide which are exposed extracellularly as indicated in Table 2. Any of the methods described above and below can be accomplished in vivo, in vitro, or ex vivo (e.g., bone marrow cells or peripheral blood lymphocytes can be treated ex vivo and then returned to the body).

5 The expression patterns of the selectively expressed polynucleotides disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by a tissue. Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of expressed sequences disclosed herein provides an example of such a tissue expression profile. It can be used as a point of reference
10 to compare and characterize samples. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue, to determine the origin of metastatic cells, to assess the physiological status of a tissue, to determine the effect of a particular treatment regime on a tissue, to evaluate the toxicity of a compound on a tissue of interest, etc.

15 For example, the tissue-selective polynucleotides disclosed herein represent the configuration of genes expressed by a normal tissue. To determine the effect of a toxin on a tissue, a sample of tissue can be obtained prior to toxin exposure ("control") and then at one or more time points after toxin exposure ("experimental"). An array of tissue-selective probes can be used to assess the expression patterns for both the control and experimental samples. As discussed in more detail below, any suitable method can be used. For instance,
20 a DNA microarray can be prepared having a set of tissue-selective genes arranged on to a small surface area in fixed and addressable positions. RNA isolated from samples can be labeled using reverse transcriptase and radioactive nucleotides, hybridized to the array, and then expression levels determined using a detection system. Several kinds of information can be extracted: presence or absence of expression, and the corresponding expression levels.
25 The normal tissue would be expected to express substantially all the genes represented by the tissue-selective probes. The various experimental conditions can be compared to it to determine whether a gene is expressed, and how its levels match up to the normal control.

30 While the expression profile of the complete gene set represented by the sequences disclosed here may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify

the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample.

Moreover, because of heterogeneity of the population, as well differences in the particular physiological state of the tissue, a tissue's "normal" expression profile is expected to differ

5 between samples, albeit in ways that do not change the overall expression pattern. As a result of these individual differences, each gene although expressed selectively in spleen, may not on its own 100% of the time be adequately enough expressed to distinguish said tissue.

Thus, the genes can be used in any of the methods and processes mentioned above and below as a group, or one at a time.

10 Binding partners can also be used as to specifically deliver therapeutic agents to a tissue of interest. For example, a gene to be delivered to a tissue can be conjugated to a binding partner (directly or through a polymer, etc.), in liposomes comprising cell surface, and then administered as appropriate to the subject who is to be treated. Additionally, cytotoxic, cytostatic, and other therapeutic agents can be delivered specifically to the tissue to
15 treat and/or prevent any of the conditions associated with the tissue of interest.

The present invention relates to methods of detecting immune system cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for a gene selected from Table 1, or a mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically to said
20 gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 3, 4, 8, 9, 14, 15, 22, 23, 27, 28, 35, 36, 42, 43, 49, 50, 57, and 58 (see, Table 5), and complements thereto.

25 Detection can also be achieved using binding partners, such as antibodies (e.g., monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting an immune system cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by gene selected from Table 1 , or
30 a mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be

accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those exposed to the surface as indicated in Table 2.

As indicated above, binding partners can be used to deliver agents specifically to the immune system, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to an immune cell can comprise, e.g., contacting an immune cell with an agent coupled to binding partner specific for a gene selected from Table 1 (i.e., TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959)), whereby said agent is delivered to said cell. Any type of agent can be used, including, therapeutic and imaging agents. Contact with the immune system can be achieved in any effective manner, including by administering effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target), present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers.

Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body. Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos, 6,264,917, 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired purpose.

The maturation of the immune system can also be modulated in accordance with the

present invention, e.g., by methods of modulating the maturation of an immune system cell, comprising, e.g., contacting said cell with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from Table 1, or a mammalian homolog thereof, whereby the maturation of an immune cell is modulated. Modulation as used throughout 5 includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

The phrase "immune system cell maturation" includes indirect or direct effects on immune system cell maturation, i.e., where modulating the gene directly effects the maturational process by modulating a gene in a immune system cell, or less directly, e.g., 10 where the gene is expressed in a cell-type that delivers a maturational signal to the immune system cell. Immune system maturation includes B-cell maturation, T-cell maturation, such as positive selection, negative selection, apoptosis, recombination, expression of T-cell receptor genes, CD4 and CD8 receptors, antigen recognition, MHC recognition, tolerization, RAG expression, differentiation, TCR expression, antigen expression, etc. See also below 15 and, e.g., Abbas et al., *Cellular and Molecular Immunology*, 4th Edition, W.B. Saunders Company, 2000, e.g., Pages 149-160. Process include reception of a signal, such as cytokinin or other GPCR ligand. Any suitable agent can be used, e.g., agents that block the maturation, such as an antibody to a GPCR of Table 1, or other GPCR antagonist.

The interactions between lymphoid and non-lymphoid immune system cells can also 20 be modulated comprising, e.g., contacting said cells with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from Table 1, or a mammalian homolog thereof, whereby the interaction is modulated. Lymphoid cells, includes, e.g., lymphocytes (T- and B-), natural killer cells, and other progeny of a lymphoid progenitor cell. Non-lymphoid cells include accessory cells, such as antigen presenting cells, macrophages, 25 mononuclear phagocytes dendritic cells, non-lymphoid thymocytes, and other cell types which do not normally arise from lymphoid progenitors. Interactions that can be modulated included, e.g., antigen presentation, positive selection, negative selection, progenitor cell differentiation, antigen expression, tolerization, TCR expression, apoptosis. See, also above and below, for other immune system processes.

30 Promoter sequences obtained from GPCR genes of the present invention can be utilized to selectively express heterologous genes in immune system cells. Methods of

expressing a heterologous polynucleotide in immune system cells can comprise, e.g., expressing a nucleic acid construct in immune system cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected from Table 5. In addition to the cell lines mentioned below, 5 the construct can be expressed in primary cells, such as thymocytes, bone marrow cells, stem cells, lymphoid progenitor cells, myeloid progenitor cells, monocytes, antigen presenting cells, macrophages, and cell lines derived therefrom, cell lines such as JHK3 (CRL-10991), KG-1 (CCL-246), KG-1a (CCL-246.1), U-937 (CRL-1593.2), VA-ES-BJ (CRL-2138), TUR (CRL-2367), ELI (CRL-9854), 28SC (CRL-9855), KMA (CRL-9856), THP-1 (TIB-2002), 10 WEHI-274.1 (CRL-1679), M-NFS-60 (CRL-1838), MH-S (CRL-2019), SR-4987 (CRL-2028), NCTC 3749 (CCL-461), AMJ2-C8 (CRL 2455), AMJ2-C11 (CRL2456), PMJ2-PC (CRL-2457), EOC2 (CRL-2467), as well as any primary and established immune system cell lines.

15 Thymus

The thymus is the site of T-cell lymphocyte maturation. Immature lymphocytes migrate into the thymus from the bone marrow and other organs in which they are generated. The selection process that shape the antigen repertoire of T-cells takes place in the thymus organ. Both positive and negative selection processes take place. For a review, see, e.g., 20 Abbas et al., *Cellular and Molecular Immunology*, 4th Edition, W.B. Saunders Company, 2000, e.g., Pages 126-130 and 149-160.

There are various diseases and disorders related to thymus tissue, including, but not limited to, thymic carcinoma, thymoma, Omenn syndrome, autoimmune diseases, allergy, Graves disease, Myasthenia gravis, thymic hyperplasia, DiGeorge syndrome, Good 25 syndrome, promoting immune system regeneration after bone marrow transplantation, immuno-responsiveness, etc. The thymic selective genes and polypeptides encoded thereby can be used to treat or diagnose any thymic condition. For instance, chemotherapeutic and cytotoxic agents can be conjugated to thymic selective antibodies and used to ablate a thymoma or carcinoma. They can be used alone or in combination with other treatments. 30 See, e.g., Graeber and Tamin, *Semin. Thorac. Cardiovasc. Surg.*, 12:268-277, 2000; Loehr, *Ann. Med.*, 31 Suppl. 2:73-79, 1999.

Bone marrow

All circulating blood cells in the adult, including all immature lymphocytes, are produced in the bone marrow. In addition, the bone marrow is also the site of B-cell maturation. The marrow consists of a spongelike reticular framework located between long trabeculae. It is filled with fat cells, stromal cells, and precursor hematopoietic cells. The precursors mature and exit through the vascular sinuses

5 All the blood cells are believed to arise from a common stem cell. Lineages that develop from this common stem cell include, e.g., myeloid and lymphoid progenitor cells. The myeloid progenitor develops into, erythrocytes (erythroid), platelets (megakaryocytic),
10 basophils, eosinophils, granulocytes, neutrophils, and monocytes. The lymphoid progenitor is the precursor to B-lymphocytes, T-lymphocytes, and natural killer cells.

There are various diseases and disorders related to bone marrow, including, not limited to, e.g., red cell diseases, aplastic anemia (e.g., where there is a defect in the myeloid stem cell), pure red cell aplasia, white cell diseases, leukopenia, neutropenia, reactive
15 (inflammatory) proliferation of white cells and nodes such as leukocytosis and lymphadenitis, neoplastic proliferation of white cells, malignant lymphoma, Non-Hodgkin's Lymphomas, Hodgkins disease, acute leukemias (e.g., acute lymphoblastic leukemia, acute myeloblastic leukemia, myelodysplastic syndrome), chronic myeloid leukemia, chronic leukemia, hairy cell leukemia, myeloproliferative disorders, plasma cell disorders, multiple myeloma,
20 histiocytoses, etc.

Immune System Selective Genes

The present invention relates to genes involved in the function and activity of the immune system. XM_062147 (TMD0088) and XM_061676 (TMD0045) code for seven membrane spanning polypeptides which are homologous to members of the olfactory G-protein-coupled receptor ("GPCR") family. XM_062147 is expressed predominantly in bone marrow tissue, with no detectable expression in other tissues. XM_061676 is also expressed predominantly in bone marrow tissue, but it is detected in peripheral blood lymphocytes, as well. As discussed in more detail below, XM_062147 (TMD0088), XM_061676 (TMD0045), and the polypeptides they encode, can be used as diagnostic, prognostic, therapeutic, and research tools for any conditions, diseases, disorders, or applications

associated with the immune system and the cells in which they are expressed.

In view of their selectivity and display on the cell surface, the GPCR family members of the present invention are useful targets for histological, diagnostic, and therapeutic applications relating to the cells (e.g., B-cells and B-cell progenitors) in which they are

5 expressed. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2 antibodies are used to breast cancer. They can also be used to detect metastatic
10 cells, in biopsies to identify bone marrow, lymphocytes, etc. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or other binding partners include those that are specific for parts of the polypeptide which are exposed extracellularly as indicated in

15 Table 2. Any of the methods described above and below can be accomplished in vivo, in vitro, or ex vivo (e.g., bone marrow cells or peripheral blood lymphocytes can be treated ex vivo and then returned to the body). Ex vivo methods can be used to eliminate cancerous cells from the bone marrow, to modulate bone marrow cells, to prime bone marrow cells for an immune response, to expand a particular class of cells expressing XM_062147
20 (TMD0088) or XM_061676 (TMD0045), to transfer genes into said cells (e.g., Banerjee and Bertino, *Lancet Oncol.*, 3:154-158, 2002), etc.

When expression is described as being "predominantly" in a given tissue, this indicates that the gene's mRNAs levels are highest in this tissue as compared to the other tissues in which it was measured. Expression can also be "selective," where expression is
25 observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold,
30 etc., or more) in that tissue when compared to other tissue-types.

The phrase "immune system" indicates any processes and cells which are involved in

generating and carrying out an immune response. Immune system cells includes, but are not limited to, e.g., stem cells, pluripotent stem cell, myeloid progenitor, lymphoid progenitor, lymphocytes, B-lymphocytes, T-lymphocytes (e.g., naive, effector, memory, cytotoxic, etc.), thymocytes; natural killer, erythroid, megakaryocyte, basophil, eosinophil, granulocyte-monocyte, accessory cells (e.g., cells that participate in initiating lymphocyte responses to antigens), antigen-presenting cells ("APC"), mononuclear phagocytes, dendritic cells, macrophages, etc., and any precursors, progenitors, or mature stages thereof.

- 5 XM_062147 contains seven transmembrane segments. It is located on chromosomal band 11q12 within proximity to the locus for an inherited form of atopic hypersensitivity
- 10 10 (OMIM 147050, e.g., associated with asthma, hay fever, and eczema). It has been suggested that the condition is a result of defect in the regulation of immunoglobulin E. XM_061676 also is seven membrane spanning polypeptide. The chromosomal locus, 11p15, to which it maps is rich in genes associated with immune disorders, including Fanconi anemia, nucleoporin, myeloid leukemia, and T-cell lymphoblastic leukemia. Arthrogryposis
- 15 15 multiplex congenita (distal type IIB) also maps closely to this chromosomal location.

The present invention relates to methods of detecting immune system cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for a gene selected from Table 6, or a mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically to said 20 gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 67, 68, 76, and 77 (see, Table 6), and complements thereto.

- 25 Detection can also be achieved using binding partners, such as antibodies (e.g., monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting an immune system cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by gene selected from Table 6, or a 30 mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be

accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc.

Useful epitopes include those exposed to the surface as indicated in Table 7.

As indicated above, binding partners can be used to deliver agents specifically to the immune system, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to an immune cell can comprise, e.g., contacting an immune cell with an agent coupled to binding partner specific for a gene selected from Table 6, whereby said agent is delivered to said cell. Any type of agent can be used, including, therapeutic and imaging agents. Contact with the immune system can be achieved in any effective manner, including by administering effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target), present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers.

Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body. Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos. 6,264,917, 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired purpose.

The maturation of the immune system can also be modulated in accordance with the present invention, e.g., by methods of modulating the maturation of an immune system cell, comprising, e.g., contacting said cell with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from Table 6, or a mammalian homolog thereof,

whereby the maturation of an immune cell is modulated. Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

The phrase "immune system cell maturation" includes indirect or direct effects on

- 5 immune system cell maturation, i.e., where modulating the gene directly effects the maturational process by modulating a gene in a immune system cell, or less directly, e.g., where the gene is expressed in a cell-type that delivers a maturational signal to the immune system cell. Immune system maturation includes B-cell maturation, T-cell maturation, such as positive selection, negative selection, apoptosis, recombination, expression of T-cell receptor genes, CD4 and CD8 receptors, antigen recognition, MHC recognition, tolerization, RAG expression, differentiation, TCR expression, antigen expression, etc. See also below and, e.g., Abbas et al., *Cellular and Molecular Immunology*, 4th Edition, W.B. Saunders Company, 2000, e.g., Pages 149-160. Processes include reception of a signal, such as cytokinin or other GPCR ligand. Any suitable agent can be used, e.g., agents that block the 10 maturation, such as an antibody to a GPCR of Table 6, or other GPCR antagonist.
- 15

The interactions between lymphoid and non-lymphoid immune system cells can also be modulated comprising, e.g., contacting said cells with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from Table 6, or a mammalian homolog thereof, whereby the interaction is modulated. Lymphoid cells, includes, e.g., lymphocytes (T- and B-), natural killer cells, and other progeny of a lymphoid progenitor cell. Non-lymphoid cells include accessory cells, such as antigen presenting cells, macrophages, mononuclear phagocytes dendritic cells, non-lymphoid thymocytes, and other cell types which do not normally arise from lymphoid progenitors. Interactions that can be modulated included, e.g., antigen presentation, positive selection, negative selection, progenitor cell 20 differentiation, antigen expression, tolerization, TCR expression, apoptosis. See, also above and below, for other immune system processes.

Promoter sequences obtained from GPCR genes of the present invention can be utilized to selectively express heterologous genes in immune system cells. Methods of expressing a heterologous polynucleotide in immune system cells can comprise, e.g., 25 expressing a nucleic acid construct in immune system cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said

promoter sequence is selected from Table 6. In addition to the cell lines mentioned below, the construct can be expressed in primary cells, such as thymocytes, bone marrow cells, stem cells, lymphoid progenitor cells, myeloid progenitor cells, monocytes, B-cells, antigen presenting cells, macrophages, and cell lines derived therefrom.

5

Kidney Selective Genes

The present invention relates to genes and polypeptides which are selectively expressed in kidney tissues: TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736),
10 TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108). These genes and polypeptides are expressed predominantly in kidney tissues, making them, and the polypeptides they encode, useful as selective markers for kidney tissue and function, as well as diagnostic, prognostic, therapeutic, and research tools for any conditions, diseases,
15 disorders, or applications associated with the kidney and the cells in which they are expressed. TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108) includes both
20 human and mammalian homologs of it. SEQ ID NOS 78-103 represent particular alleles, but the present invention relates to other alleles, including naturally-occurring polymorphisms (i.e., a polymorphism in the nucleotide sequence which is identified in populations of mammals) and homologs thereof. More information on these genes is summarized in Tables 8-11.
25 In view of their selectivity and display on the cell surface, the polypeptides and polynucleotides of the present invention are useful targets for histological, diagnostic, and therapeutic applications relating to the cells (e.g., juxtaglomerular cells which secrete renin, peritubular cells, endothelial cells, e.g., of the cortex and outer medulla, mesangial cells which secrete inflammatory mediators including NO and products of cyclooxygenase,
30 visceral epithelial cells, parietal epithelial cells, podocytes, early proximal tubule cells which secrete, e.g., angiotensin converting enzyme and neutral endopeptidase, late distal tubule

cells that produce, e.g., prolyl endopeptidase, serine endopeptidase, carboxypeptidase, and neutral endopeptidase, renomedullary interstitial cells, etc) in which they are expressed. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited 5 to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2, antibodies are used to breast cancer. They can also be used to detect metastatic cells, in biopsies, to identify kidney, etc. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, 10 to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or other binding partners include those that are specific for parts of the polypeptide which are exposed extracellularly as indicated in Table 9. Any of the methods described above and below can be accomplished in vivo, in vitro, or ex vivo.

When expression is described as being "predominantly" in a given tissue, this 15 indicates that the gene's mRNAs levels are highest in this tissue as compared to the other tissues in which it was measured. Expression can also be "selective," where expression is observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript 20 is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, etc., or more) in that tissue when compared to other tissue-types.

The present invention relates to methods of detecting kidney cells, comprising one or 25 more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), or a mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically 30 to said gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below,

such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 104, 105, 107, 108, 111, 112, 115, 116, 119, 120, 122, 123, 126, 127, 131, 132, 135, 136, 138, 139, 142, 143, 145, 146, 149, 150, and complements thereto.

Detection can also be achieved using binding partners, such as antibodies (e.g., 5 monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting a kidney cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by TMD0049 (XM_057351), TMD0190 10 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), or a mammalian homolog thereof, under conditions effective for said binding 15 partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those exposed to the surface as indicated in Table 9.

As indicated above, binding partners can be used to deliver agents specifically to the kidney, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an 20 agent to a kidney cell can comprise, e.g., contacting a kidney cell with an agent coupled to binding partner specific for TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), whereby said 25 agent is delivered to said cell. Any type of agent can be used, including, therapeutic and imaging agents. Contact with the kidney can be achieved in any effective manner, including by administering effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried 30 specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target),

present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers. Any cell expressing a polypeptide coded for by TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, 5 TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108) can be targeted, including, e.g., juxtaglomerular, peritubular, endothelial, mesangial, visceral epithelial, parietal epithelial, podocytes, early proximal tubule, late distal tubule, renomedullary interstitial, etc.

10 Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body. Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with 15 binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos. 6,264,917, 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired 20 purpose.

A kidney cell (see above for examples of kidney cell types) can also be modulated in accordance with the present invention, e.g., by methods of modulating a kidney cell, comprising, e.g., contacting said cell with an agent effective to modulate TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 25 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), or the biological activity of a polypeptide encoded thereby, or a mammalian homolog thereof, whereby said kidney cell is modulated. Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, 30 amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

An activity or function of the kidney cell can be modulated, including, e.g., glomerular filtration rate, filtration pressure, renal autoregulation (including via myogenic mechanism and tubuloglomerular feedback mechanism), tubular reabsorption, tubular secretion, and renal clearance. In addition, the transcription, translation, synthesis, degradation, expression, etc., of any secretory or polypeptide produced by a kidney cell can be modulated, including, but not limited to, renin-angiotensin activity, production and secretion of prostaglandins, nitric oxide, kallikrein, adenosine, endothelin, erythropoietin, and other hormones, enzymes, and other secretory and intracellular factors. The response of a kidney cell to stimuli can also be modulated, including, but not limited to, ligands to TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), oxygen levels, blood pressure, etc.

The present invention also relates to polypeptide detection methods for assessing kidney function, e.g., methods of assessing kidney function, comprising, detecting a polypeptide coded for by TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108), fragments thereof, polymorphisms thereof, in a body fluid, whereby the level of said polypeptide in said fluid is a measure of kidney function. Kidney function tests are usually performed to determine whether the kidney is functioning normally as a way of diagnosing kidney disease. Various tests are commonly used, including, e.g., BUN (blood urea nitrogen), serum creatinine, estimated GFR, ability to concentrate urine, BUN/creatinine ratio, urine sodium and other electrolytes, urine NAG (N-acetyl-beta-glucosaminidase, adenosine deaminase, urinary alkaline phosphatase, serum and urine beta-2-microglobulin, serum uric acid, isotope scans, Doppler sonogram, positron emission tomography, specific gravity of urine, microalbumin, total protein, etc. Detection of TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148

(XM_087108) provides an additional assessment tool, especially in diseases such as chronic renal failure, urinary tract infections, kidney stones, nephrotic syndrome, nephritic syndrome, kidney disease due to diabetes or high blood pressure, etc., As with the other tests, elevated levels of said polypeptide in blood, or other fluids, can indicate impaired kidney function.

- 5 Values can be determined routinely, as they are for other kidney function markers, such as those mentioned above. Detecting can be performed routinely (see below), e.g., using an antibody which is specific for said polypeptide, by RIA, ELISA, or Western blot, etc.

Promoter sequences obtained from genes of the present invention can be utilized to selectively express heterologous genes in kidney cells. Methods of expressing a heterologous

- 10 polynucleotide in kidney cells can comprise, e.g., expressing a nucleic acid construct in kidney cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected SEQ ID NOS 106, 109, 110, 113, 114, 117, 118, 121, 124, 125, 128-130, 133, 134, 137, 140, 141, 144, 147, 148, and 151. In addition to the cell lines mentioned below, the construct can be expressed in
- 15 primary cells or in established cell lines.

Kidney

The kidney maintains the constancy of fluids in an organism's internal environment, and is therefore of great importance in maintaining health and vitality. Each day, the kidney

- 20 filters the blood, removing and concentrating toxins, metabolic wastes, and excess ions, allowing them to be excreted by the body in the form of urine. The excretory function of the kidney is performed by over one million blood units called nephrons, each a miniature blood filtering and processing unit. A nephron consists of a glomerulus, a tuft of capillaries, and a renal tubule. In addition to their excretory function, kidneys produce a number of different
- 25 hormones, enzymes, and other secreted molecules, including the enzyme renin and the hormone erythropoietin. The kidney also is responsible for metabolizing vitamin D into its active form, calcitriol. For a full description of the kidney's function and structure, see, e.g., *Human Anatomy and Physiology*, Marieb, E.N., 3rd Edition, Benjamin/Cummings Publishing Company, Inc., 1995, pp 896-923.

- 30 The glomerulus is a high pressure capillary bed which filters out most substances smaller than large plasma proteins across the fenestrated glomerular epithelium, the

intervening basement membrane, and the podocyte-containing visceral membrane of the glomerulus capsule. The external layer of the glomerulus is called the parietal layer, consisting predominately of a squamous epithelium. This layer is structural. Underneath it, is the visceral layer which consists of the modified branching epithelial cells called podocytes.

- 5 These sit on top of the fenestrated glomerular endothelium. The glomerulus is connected to the renal tubule, a highly differentiated and long tube, having three major elements: the proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule. Different regions of the tubule have different functions in absorption and secretion.

Renal cells produce a variety of different hormones and chemicals, including,

- 10 prostaglandins, nitric oxide, kallikrein family, adenosine, endothelin family, renin, erythropoietin, aldosterone, antidiuretic hormone (vasopressin), natriuretic hormones, etc. Renin is involved in modulating blood pressure. It cleaves angiotensinogen, a plasma peptide, splitting off a fragment containing 10 amino acids called angiotensin I. Angiotensin I is cleaved by a peptidase secreted by blood vessels called angiotensin converting enzyme
- 15 (ACE), producing angiotensin II, which contains 8 amino acids. Angiotensin II has many direct effects on blood pressure. Erythropoietin stimulates red blood cell production in the bone marrow.

TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369),
TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719
20 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841
(XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108) can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of the kidney. These include, but are not limited to, diseases that affect the four basic morphologic components, glomeruli, tubules, interstitium, and blood vessels. Diseases
25- include, e.g., acute nephritic syndrome, nephritic syndrome, renal failure, urinary tract infections, renal stones, cystic diseases of the kidney, e.g., cystic renal dysplasia, polycystic disease (autosomal dominant and recessive types), medullary cystic disease, acquired cystic disease, renal cysts, parenchymal cysts, perihilar renal cysts (pyelocalyceal cysts, hilar lymphangitic cysts), glomerular diseases, diseases of tubules, tubulointerstitial diseases,
30 tumors of the kidney, such as benign tumors (cortical adenoma, renal fibroma, renomedullary interstitial cell tumor), malignant tumors (renal cell carcinoma, hypernephroma,

adenocarcinoma of kidney, Wilms' tumor, nephroblastoma, urothelial carcinoma), renal coloboma, nephroblastoma, clear cell sarcoma of kidney (CCSK), rhabdoid tumor of kidney (RTK), von Hippel-Lindau disease, oncocyoid renal cell carcinoma (RCC), renal leiomyoblastoma, etc. TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242

- 5 (XM_088369), TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841 (XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108) can also be used for staging and classifying conditions and diseases of the present invention, alone, or in combination with conventional staging and classification schemes.

10

Pancreatic Gene Complex

The present invention relates to a cluster of olfactory GPCR (G-protein coupled) receptor genes located at chromosomal band 11q24. These genes are expressed predominantly in pancreatic tissue, establishing this region of chromosome 11 as a unique gene complex involved in pancreatic function. See, Table 12. Because of their exquisite selectivity for pancreatic tissues, the pancreatic gene complex ("PGC"), and the genes which comprise it, are useful to assess pancreas tissue and function for diagnostic, prognostic, therapeutic, and research purposes.

The spatial organization of the pancreatic gene complex ("PGC") is illustrated in Fig.

- 20 7. It spans several hundred kilobases of chromosome 11, e.g., from about LOC160205 to LOC119954, from about LOC119944-LOC119954, and any part thereof. Within this region, is a cluster of genes coding for polypeptides which share sequence identity with the olfactory GPCR family. These include, but are not limited to, TMD0986, XM_061780 (TMD0987), XM_061781 (TMD0353), XM_061784 (TMD0989), XM_061785 (TMD058). Fig. 8
25 illustrates the relationship between the lengths of the different coding sequences. As shown in the figure, XM_061784 is shorter at its C-terminus than the other family members.

As members of the GPCR family, the PGC genes all share a degree of amino acid sequence identity and similarity. See, Table 14 for values (% sequence identity is the first place; % sequence similarity is in parenthesis in the second place; calculations were

- 30 performed using the publicly-available BLASTP pair-wise alignment program). TMD0986, XM_061780, XM_061781, and XM_061785 each share about 40% sequence identity.

BLAST searching of publicly available sequences indicates that these polypeptides share less amino acid sequence identity with each other than they do with other olfactory GPCR homologs located elsewhere in the genome. Significantly higher amino acid sequence identity – 81% – is observed between the adjacent genes XM_061784 and XM_061785.

- 5 These genes appear to be part of a sub-cluster within PGC that share high polypeptide similarity between them.

The phrase “a gene of Table 12” which is used throughout the description include the specific sequences for the listed XM numbers as well as other human alleles, and mammalian homologs, such as murine homologs. For example, Table 14 lists several of the mouse 10 homologs that are included in the present invention. While SEQ ID NOS. 152, 153, 162, 163, 167, 168, 171, 172, 175, and 176 may represent particular alleles, the present invention relates to other alleles, as well, including naturally-occurring polymorphisms (i.e., a polymorphism in a nucleotide sequence which is identified in populations of mammals).

TMD0986 (SEQ ID NO 152 and 153) is a full-length sequence of the previously 15 identified XM_061779. It contains an additional 117 amino acids not present in XM_061779. The present invention relates to nucleic acids comprising or consisting essentially of this sequence in its entirety (e.g., amino acids 1-314), comprising or consisting essentially of nucleic acids coding for amino acids 1-117, and comprising or consisting essentially of fragments of nucleic acids coding for amino acids 1-117. Polypeptides 20 encoded by these nucleic acids are also claimed, including polypeptide fragments of 1-117, such as 1-23, 79-97, 164-198, 261-274, and other extracellularly exposed peptides. In addition, the present invention relates to binding partners, such as antibodies, that bind to epitopes within amino acids 1-117 (e.g., SEQ ID NO 153).

25 **Pancreas**

Diabetes and other pancreatic disorders are a major health concern. Worldwide, it is estimated that 5-10% of the population suffers from some form of diabetes. Pancreatic cancer is the fifth leading cause of cancer-related mortality. In 2002, it was estimated that about 30,000 Americans would be diagnosed with pancreatic cancer, and 90% would die 30 within 12 months. Despite the prevalence of pancreatic disease, the genetics and physiology of normal pancreatic function and pancreatic disease is still poorly understood.

The pancreas is a mixed gland comprised of exocrine and endocrine tissues. The exocrine portion comprises about 80-85% of the organ. It is divided into lobes by connective tissue septa, and each lobe is divided into several lobules. These lobules are composed of grape-like clusters of secretory cells that form sacs known as acini. An acinus is a functional unit of the pancreatic exocrine gland. All acini drain into interlobular ducts which merge to form the main pancreatic duct. It, in turn, joins together with the bile duct from the liver to form the common bile duct that empties into the duodenum. Pancreatic acinar cells make up more than 80% of the total volume of the pancreas and function in the secretion of the various enzymes that assist digestion in the gastrointestinal tract. Scattered among the acinar cells are approximately a million pancreatic islets ("islets of Langerhans") that secrete the pancreatic endocrine hormones. These dispersed islets comprise approximately 2% of the total volume of the pancreas.

The basic function of the pancreatic endocrine cells is to secrete certain hormones that participate in the metabolism of proteins, carbohydrates, and fats. The hormones secreted by the islets include, e.g., insulin, glucagon, somatostatin, pancreatic polypeptide, amylin, adrenomedullin, gastrin, secretin, and peptide-YY. See, also, Shimizu et al., *Endocrin.*, 139:389-396, 1998. The islets contain about four major and two minor cell types. The major cell types are alpha (glucagon producing), beta (insulin and amylin producing), delta (somatostatin producing which suppresses both insulin and glucagon release), and F (pancreatic polypeptide and adrenomedullin producing) cells. The minor cell types are D1 (produce vasoactive intestinal peptide or VIP) and enterochromaffin (produce serotonin) cells. The cells can be distinguished, e.g., by their morphology, hormonal content, and polynucleotide expression patterns.

The ability of the pancreas to respond to a wide variety of metabolic signals is conferred by an expression profile comprising a rich assortment of receptor proteins. G-protein coupled receptors have been previously identified in the pancreas, including, e.g., receptors for glucagon, secretin, CCK (e.g., Roettger et al., *J. Cell Biol.*, 130:579-590, 1995), purines (e.g., P2 purinoreceptors); gastrin, KiSS-1 peptides (e.g., Kotani et al., *J. Biol. Chem.*, 276:34631-6, 2001), adrenomedullin (Martinez et al., *Endocrin.*, 141:406, 2000), and interleukins. G-protein subunits have also been localized to the pancreas, including G-proteins which were previously associated with the olfactory epithelium. See, e.g., Zigman et

al., *Endocrin.*, 133:2508-2514, 1993. In addition, pancreatic cells express neurotropin, neurotensin, and interleukin receptors.

As mentioned, the pancreas is sensitive to a variety of metabolic, soluble and hormonal signals involved in regulating blood sugar, modulating synthesis and release of 5 pancreatic digestive enzymes, and other physiologically important processes involved in pancreas function. In analogy to the ability of olfactory receptors to detect odors and pheromones in the environment, the pancreatic GPCRs of the present invention can be used to "sniff" out and respond to various ligands in the blood which pass through the pancreas, including peptides, metabolites, and other biologically-active molecules. Biological activities 10 include, but are not limited to, e.g., regulation of blood sugar, modulation of all aspects of the various secreted polypeptides (hormones, enzymes, etc.) produced by the pancreas, ligand-binding, exocytosis, amylase (and any of the other 20 or so digestive enzymes produced by the pancreas) secretion, autocrine responses, apoptosis (e.g., in the survival of beta-islet cells), zymogen granule processing, G-protein coupling activity, etc.

15 The polynucleotides, polypeptides, and ligands thereto, of the present invention can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of pancreas. These include, but are not limited to, e.g., disorders associated with loss or mutation to 11q24, such as Jacobsen syndrome (OMIM #147791), cystic fibrosis, acute and chronic pancreatitis, pancreatic abscess, pancreatic pseudocyst, 20 nonalcoholic pancreatitis, alcoholic pancreatitis, classic acute hemorrhagic pancreatitis, chronic calcifying pancreatitis, familial hereditary pancreatitis, carcinomas of the pancreas, primary (idiopathic) diabetes (e.g., Type I (insulin dependent diabetes mellitus, IDDM) [insulin deficiency, beta cell depletion], Type II (non-insulin dependent diabetes mellitus, NIDDM) [insulin resistance, relative insulin deficiency, mild beta cell depletion]), nonobese 25 NIDDM, obese NIDDM, maturity-onset diabetes of the young (MODY), islet cell tumors, diffuse hyperplasia of the islets of Langerhans, benign adenomas, malignant islet tumors, hyperfunction of the islets of Langerhans, hyperinsulinism and hypoglycemia, Zollinger-Ellison syndrome, beta cell tumors (insulinoma), alpha cell tumors (glucagonoma), delta cell tumors (somatostatinoma), vipoma (diarrheogenic islet.cell tumor), pancreatic cancers, 30 pancreatic carcinoid tumors, multihormonal tumors, multiple endocrine neoplasia (MEN), MEN I (Wermer syndrome), MEN II (Sipple syndrome), MEN III or IIb, pancreatic endocrine

tumors, etc.

In view of its selectivity and display on the cell surface, the olfactory GPCR family members of the present invention are useful targets for histological, diagnostic, and therapeutic applications relating to the cells (e.g., pancreatic progenitor, exocrine, endocrine, 5 acinar, islet; alpha, beta, delta, F, D1, enterochromaffin, etc.) in which they are expressed.

Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited

to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2

10 antibodies are used to breast cancer. They can also be used to detect metastatic cells, in biopsies to identify bone marrow, lymphocytes, etc. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or other binding partners include those that are

15 specific for parts of the polypeptide which are exposed extracellularly as indicated in Table 14. Any of the methods described above and below can be accomplished *in vivo*, *in vitro*, or *ex vivo*.

When expression is described as being "predominantly" in a given tissue, this indicates that the gene's mRNAs levels are highest in this tissue as compared to the other 20 tissues in which it was measured. Expression can also be "selective," where expression is observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, etc., or more) in that tissue when compared to other tissue-types.

The present invention relates to methods of detecting pancreas cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for a gene of Table 12, or a mammalian homolog thereof, under 30 conditions effective for said polynucleotide to hybridize specifically to said gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and

technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 154, 155, 164, 165, 169, 170, 173, 174, 177, and 178, and complements thereto.

Detection can also be achieved using binding partners, such as antibodies (e.g., 5 monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting a pancreas cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by a polypeptide of Table 12, or a 10 mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those exposed to the surface as indicated in Table 14.

As indicated above, binding partners can be used to deliver agents specifically to the 15 pancreas, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to a pancreas cell can comprise, e.g., contacting a pancreas cell with an agent coupled to a binding partner specific for a polypeptide coding for a gene of Table 12, whereby said agent is delivered to said cell. Any type of agent can be used, including, therapeutic and imaging agents. Contact with the pancreas can be achieved in any effective manner, 20 including by administering effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target), 25 present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers. Any cell expressing a polypeptide coded for by a gene of Table 12 can be targeted, including, e.g., pancreatic progenitor, exocrine, endocrine, secretory, acinar, islet, alpha, beta, delta, F, D1, enterochromaffin, etc.

30 Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body.

Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos. 6,264,917, 5 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired purpose. See, Bruehlmeier et al., *Nucl. Med. Biol.*, 29:321-327, 2002, for imaging pancreas 10 using labeled receptor ligands. Antibodies and other ligands to receptors of the present invention can be used analogously.

A pancreas cell (see above for examples of pancreas cell types) can also be modulated in accordance with the present invention, e.g., by methods of modulating a pancreas cell, comprising, e.g., contacting said cell with an agent effective to modulate a gene of Table 12, 15 or the biological activity of a polypeptide encoded thereby (e.g., SEQ ID NO 153, 163, 168, 172, or 176), or a mammalian homolog thereof, whereby said pancreas cell is modulated. Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

20 An activity or function of the pancreas cell can be modulated, including, e.g., regulation of blood sugar, modulation of all aspects of the various secreted polypeptides (hormones, enzymes, etc.) produced by the pancreas, ligand-binding, exocytosis, amylase (and any of the other 20 or so digestive enzymes produced by the pancreas) secretion, autocrine responses, apoptosis (e.g., in the survival of beta-islet cells), etc.

25 The present invention also relates to polypeptide detection methods for assessing pancreas function, e.g., methods of assessing pancreas function, comprising, detecting a polypeptide coded for by a gene of Table 12, fragments thereof, polymorphisms thereof, in a body fluid, whereby the level of said polypeptide in said fluid is a measure of pancreas function. Pancreas function tests are usually performed to determine whether the pancreas is 30 functioning normally as a way of diagnosing pancreas disease. Various tests are commonly used, including, e.g., assays for the presence of pancreatic enzymes in body fluids (e.g.,

amylase, serum lipase, serum trypsin-like immunoactivity), studies of pancreatic structure (e.g., using x-ray, sonography, CT-scan, angiography, endoscopic retrograde cholangiopancreatography), and tests for pancreatic function (e.g., secretin-pancreozymin (CCK) test, Lundh meal test, Bz-Ty-PABA test, chymotrypsin in feces, etc). Detection of a 5 polypeptide coded for by a gene of Table 12 provides an additional assessment tool, especially in diseases such as pancreatitis and pancreatic cancer where pancreatic markers can appear in the blood, stool, urine, and other body fluids. As with the other tests, elevated levels of said polypeptide in blood, or other fluids, can indicate impaired pancreas function. Values can be determined routinely, as they are for other markers , such as those mentioned 10 above. Detecting can be performed routinely (see below), e.g., using an antibody which is specific for said polypeptide, by RIA, ELISA, or Western blot, etc., in analogy to the tests for pancreatic enzymes in body fluids.

Promoter sequences obtained from GPCR genes of the present invention can be utilized to selectively express heterologous genes in pancreas cells. Methods of expressing a 15 heterologous polynucleotide in pancreas cells can comprise, e.g., expressing a nucleic acid construct in pancreas cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected SEQ ID NOS 156-161, 166, 179, or 180. In addition to the cell lines mentioned below, the construct can be expressed in primary cells or in established cell lines.

20 The genes and polypeptides of Table 12 can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of the pancreas as mentioned above. The present invention relates to methods of identifying a pancreatic disease or pancreatic disease-susceptibility, comprising, e.g., determining the association of a pancreatic disease or pancreatic disease-susceptibility with a nucleotide 25 sequence present within the pancreatic gene complex. An association between a pancreas disease or disease-susceptibility and nucleotide sequence includes, e.g., establishing (or finding) a correlation (or relationship) between a DNA marker (e.g., gene, VNTR, polymorphism, EST, etc.) and a particular disease state. Once a relationship is identified, the DNA marker can be utilized in diagnostic tests and as a drug target.

30 Any region of the pancreatic gene complex can be used as a source of the DNA marker (e.g., a nucleotide sequence present with PGC), including, e.g., TMD0986,

XM_061780 (TMD0987), XM_061781 (TMD0353), XM_061784 (TMD0989), XM_061785 (TMD058), and any part thereof, introns, intergenic regions, any DNA from about 29160-29310 kb of 11q24, NT_009215, etc.

Human linkage maps can be constructed to establish a relationship between a region

- 5 within 11q24 and a pancreatic disease or condition. Typically, polymorphic molecular
markers (e.g., STRP's, SNP's, RFLP's, VNTR's) are identified within the region, linkage
and map distance between the markers is then established, and then linkage is established
between phenotype and the various individual molecular markers. Maps can be produced
individual family, selected populations, patient populations, etc. In general, these methods
10 involve identifying a marker associated with the disease (e.g., identifying a polymorphism in
a family which is linked to the disease) and then analyzing the surrounding DNA to identify
the gene responsible for the phenotype.

Retina Selective Gene

- 15 The present invention relates to NM_013941 (GPCR181 or OR10C1), a multiple
transmembrane spanning polypeptide which shares sequence identity with the olfactory G-
protein coupled receptor (GPCR) family. Like other GPCR, NM_013941 has seven
transmembrane domains, at about amino acid positions 20-42, 54-76, 91-113, 134-156, 190-
212, 233-255, and 265-287, of SEQ ID NO 182. It is located at about chromosomal band
20 6p21.31-22.2. There are several other GPCRs located nearby (e.g., OR2B3, AL022727;
OR2J3, AL022727). NM_013941 is highly expressed in brain tissue, at lower levels in heart,
pituitary, and skin, and at minimally detectable levels in colon, small intestine, kidney,
lymphocytes, and mammary gland. In the neuronal tissue, it was selectively expressed in the
retina, but was not detected in any other brain tissue regions. The selective expression of
25 NM_013941 in the retina makes it useful as a marker for retinal tissue, e.g., in stem cell
cultures and biopsy samples, as well as a diagnostic, prognostic, therapeutic, and research
tool for any conditions, diseases, disorders, or applications associated with the retina and the
cells in which it is expressed. NM_013941 includes both human and mammalian homologs
of it (e.g., mouse XM_111729 which is similar to olfactory receptor MOR263-6). SEQ ID
30 NOS. 181 and 182 represent a particular allele of NM_013941; the present invention relates
to other alleles, as well, including naturally-occurring polymorphisms (i.e., a polymorphism
in the nucleotide sequence which is identified in populations of mammals).

The chromosomal region within which NM_013941 is located comprises a number of genes involved in retinal function. These include, e.g., retinal cone dystrophy (OMIM 602093) which appears to be a result of mutation in guanylate cyclase activator-1A (e.g., Payne et al., *Human Molec. Genet.*, 7:273-277, 1998), retinal degeneration slow (OMIM 179605) which appears to be a defect in specific retinal protein homologous to rod outer segment protein-1, retinitis pigmentosa-7, retinitis pigmentosa-14 (OMIM 600132) which is associated with a mutation in the tubby-like protein TULP1 (e.g., Banerjee et al., *Nature Genet.*, 18:177-179, 1998; Hagstrom et al., *Nature Genet.*, 18:174-176, 1998), and others. Thus, this region appears to be important in eye function.

In view of its selectivity and display on the cell surface, the olfactory GPCR family members of the present invention are useful targets for histological, diagnostic, and therapeutic applications relating to retinal cells. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat retinal carcinomas (e.g., retinoblastoma) in analogy to how c-erbB-2 antibodies are used to breast cancer. See, e.g., Hayashi et al., *Invest. Ophthalmol. Vis. Sci.*, 40:265-72, 1999 for an example treating retinoblastoma using HSV-TK. Transfer of the gene into the retinal cells can be achieved by incorporating the gene into liposomes which have been made cell-selective by incorporating a NM_013941 specific antibody into its bilayer. See, also, Wu and Wu, *J. Biol. Chem.*, 262: 4429-4432, 1987.

The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or other binding partners include those that are specific for parts of the polypeptide which are exposed extracellularly. Any of the methods described above and below can be accomplished *in vivo*, *in vitro*, or *ex vivo*.

When expression is described as being "predominantly" in a given tissue, this indicates that the gene's mRNAs levels are highest in this tissue as compared to the other tissues in which it was measured. Expression can also be "selective," where expression is observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule

comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, 5 etc., or more) in that tissue when compared to other tissue-types.

The present invention relates to methods of detecting retinal cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for NM_013941 (e.g., SEQ ID NOS 181), or a mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically to said gene, and 10 detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 183 and 184, and complements thereto.

Detection can also be achieved using binding partners, such as antibodies (e.g., 15 monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting a retinal cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by NM_013941 (e.g.; SEQ ID NO 182), or a 20 mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those exposed to the surface.

As indicated above; binding partners can be used to deliver agents specifically to the 25 retina, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to a retinal cell can comprise, e.g., contacting a retinal cell with an agent coupled to binding partner specific for NM_013941 (SEQ ID NO 182), whereby said agent is delivered to said cell. Any type of agent can be used, including, therapeutic and imaging agents. Contact with the retinal can be achieved in any effective manner, including by administering 30 effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent

is associated with the binding partner in such a manner that it can be carried specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target), present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can

- 5 be directly linked to the binding partner, or via chemical linkers or spacers. Any cell expressing a polypeptide coded for by NM_013941 can be targeted, including, e.g., pigmented epithelial cells, photoreceptor cells, cones, rods, bipolar cells, ganglion cells, etc.

Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body.

- 10 Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos, 6,264,917, 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators,
- 15 radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired purpose.

- A retinal cell (see above for examples of retinal cell types) can also be modulated in accordance with the present invention, e.g., by methods of modulating a retinal cell, comprising, e.g., contacting said cell with an agent effective to modulate NM_013941, or the biological activity of a polypeptide encoded thereby (e.g., SEQ ID NO 182), or a mammalian homolog thereof, whereby said retinal cell is modulated. Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

- Any activity or function of the retinal cell can be modulated, including, e.g., light reception, phototransduction, excitation of rods, excitation of cones, metabolism of vitamin A, retinal, rhodopsin, and other functional molecules, cGMP binding and hydrolysis, sodium channel flux, membrane potential, phosphodiesterase activity, G-protein activity and coupling, vitamin A processing, sodium pump activity, calcium flux, etc. The response of a retinal cell to stimuli can also be modulated, including, but not limited to, ligands to

NM_013941, light, ion levels, second messenger levels, etc.

Promoter sequences can be utilized to selectively express heterologous genes in retinal cells. Methods of expressing a heterologous polynucleotide in retinal cells can comprise, e.g., expressing a nucleic acid construct in retinal cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is obtained from NM_01394, e.g., on genomic NT_007592. In addition to the cell lines mentioned below, the construct can be expressed in primary cells or in established cell lines.

10 Retina

The retina is a two-layered structure located on the back of the eye. It is the primary organ responsible for vision. The outer pigmented layer is comprised of pigmented epithelial cells that absorb light, preventing it from scattering in the eye, and store vitamin A needed by the photoreceptor cells. The inner neural layer is comprised of three main cell types: photoreceptor cells, bipolar cells, and ganglion cells. The local currents generated by a light stimulus spreads from the photoreceptor cells to the bipolar cells, and then on to the innermost ganglion cells. The optic disc is the exit site of the retinal ganglion axons which then bundle into the optic nerve

Photoreceptors consist of rods and cones which are the photosensitive cells of the retina. Each rod and cone elaborates a specialized cilium, called the outer segment, that contains the phototransduction machinery. The rods contain a specific light-absorbing visual pigment, rhodopsin. In humans, there are three classes of cones, each characterized by the expression of distinct visual pigments: the blue cone, green cone and red cone pigments. Each type of visual pigment protein is tuned to absorb light maximally at different wavelengths. The rod rhodopsin mediates scotopic vision (in dim light), whereas the cone pigments are responsible for photopic vision (in bright light). The red, blue and green pigments also form the basis of color vision.

NM_013941 can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of the retinal. These include, but are not limited to, diseases that affect the basic morphologic components as mentioned above, e.g., the outer and inner cell layers, and the optic nerve the retina. Diseases include, e.g.,

retinal degeneration, retinal degenerations such as retinitis pigmentosa, Bardet-Biedl syndrome, Bassen-Kornzweig syndrome (abetalipoproteinemia), Best disease (vitelliform dystrophy), choroideremia, gyrate atrophy, congenital amaurosis, Refsum syndrome, Stargardt disease, Usher syndrome, macular degeneration (dry and wet forms), diabetic retinopathy, 5 peripheral vitreoretinopathies, photic retinopathies, surgery-induced retinopathies, viral retinopathies (such as HIV retinopathy related to AIDS), ischemic retinopathies, retinal detachment, traumatic retinopathy, optic neuropathy, optic neuritis, ischemic optic neuropathy, Leber optic neuropathy, diseases of Bruch's membrane, glaucoma, cancer, retinoblastoma, cancer- associated retinopathy syndrome (CAR syndrome), melanoma- 10 associated retinopathy (MAR), etc. NM_013941 can also be used for staging and classifying conditions and diseases of the present invention, alone, or in combination with conventional staging and classification schemes.

Spleen Gene Cluster

15 The present invention relates to a cluster of transmembrane and GPCR-type receptor genes located at chromosomal band 11q12.2. The genes of the present invention are expressed predominantly in the spleen (e.g., Fig. 10, lane 19) (hence, "spleen gene" cluster), as well as other tissues of the immune and reticuloendothelial system (RES), establishing this region of the chromosome as a unique gene complex involved in spleen, lymphoid, and/or 20 reticuloendothelial function. TMD1030 and TMD0621 are highly expressed in spleen tissue, with insignificant levels in other tissues. In addition to spleen, TMD1029 and TMD1029 show significant expression in the liver and lymphocytes, as well. Because of their selectivity for spleen, lymphoid, and/or reticuloendothelial tissues, the gene complex, and the chromosomal region which comprises it, are useful to assess spleen, lymphoid, and/or 25 reticuloendothelial tissue function and for diagnostic, prognostic, therapeutic, and research purposes. Information on the genes is summarized in Tables 15-19.

The spatial organization of the gene complex is illustrated in Fig. 11. The complex spans about at least 100 kb, from about EST markers G62658, SHGC-82134, etc. (located at the end closest to the centromere and TMD1030) to SHGC-154002, SHGC-9433, etc.

30 (located at the end furthest from the centromere and TMD0621). All the genes have the same orientation of transcription. TMD1799 (XM_166849) (SEQ ID NO 193-194), located at the

upper region, shows very high expression in lymphocytes, but only marginal expression in spleen, indicating that expression in lymphocytes may predominate at the boundaries of the gene complex. In the lower region, TMD1027 (XM_166856) (SEQ ID NO 195-196), spleen expression virtually disappears, while lymph node expression becomes very high. The 5 present invention includes this entire region, and any parts thereof. For instance, the present invention includes any DNA fragments within it which confer the observed tissue specificities described herein.

The gene complex is involved in spleen, immune, and RES functions. The spleen is located in the left upper region of the abdomen. In the adult, it weights about 90-180 grams, and is about 15 by 7.5 cm in size. The spleen is anatomically and functionally compartmentalized into two distinct regions, the red and white pulp. The red pulp comprises blood vessels interwoven with connective tissue ("pulp cords") that is lined with reticuloendothelial cells. It possesses a blood filtering function, removing opsonized cells and trapping abnormal red blood cells. It also is a storage reservoir for platelets and other blood cells. In the fetus, the red pulp has a hematopoietic function. 10 Inside the red pulp, is lymphoid tissue known as the white pulp. Antibodies are made inside the white pulp. Similar to other lymphatic tissues, B- and T-cell's mature inside the white pulp, where they are involved in antigen presentation and lymphocyte maturation. The white pulp is clustered around the periarteriolar lymphoid sheath, and is comprised of follicles and marginal zone. 15 Naive B-cells are located in the primary follicle, memory cells, macrophages, and dendritic cells in the secondary follicle, and macrophages and B-cells in the marginal zone. The integrins LFA-1 and alpha4-beta1 are involved in localization of the B-cells to the marginal zone of the white pulp 20 (Lu and Cyster, *Science*, 297:409, 2002).

The reticuloendothelial system (RES) is a multi-organ phagocytic system involved in removing particulates from the blood. It is comprised of the spleen and liver. It has the 25 ability to sequester inert particles and dyes. Cells of the RES system include, macrophages, liver Kuppfer cells, endothelial cells lining the sinusoids of the liver, spleen, and bone marrow, and reticular cells of lymphatic and bone marrow tissues.

The polynucleotides, polypeptides, and ligands thereto, of the present invention can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., 30 diseases and conditions of spleen, lymphoid, and/or reticuloendothelial tissues. These include, but are not limited to, splenomegaly, hypersplenism, hemolytic anemis, hereditary

spherocytosis, hereditary elliptocytosis, thalassemia minor and major, autoimmune hemolytic anemia, thrombocytopenia, idiopathic thrombocytopenic purpura, immunologic thrombocytopenia associated with chronic lymphocytic leukemia or systemic lupus erythematosis, TTP, leukemia, lymphoma, primary and metastatic tumors, splenic cysts, 5 infection, inflammatory diseases, anemias, blood cancers, etc. See, Table 19 for other examples.

In view of their selectivity and display on the cell surface, the genes of the present invention are useful targets for histological, diagnostic, and therapeutic applications relating to the cells (e.g., reticuloendothelial cells, macrophages, Kupffer cells, monocytes, B- 10 lymphocytes, T-lymphocytes, etc) in which they are expressed. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2 antibodies are used to 15 treat breast cancer. They can also be used to detect metastatic cells in biopsies. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or other binding partners include those that are specific for parts of the polypeptide which are exposed extracellularly. 20 See, Table 16. Any of the methods described above and below can be accomplished in vivo, in vitro, or ex vivo.

When expression is described as being "predominantly" in a given tissue, this indicates that the gene's mRNAs levels are highest in this tissue as compared to the other tissues in which it was measured. Expression can also be "selective," where expression is 25 observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, 30 etc., or more) in that tissue when compared to other tissue-types. TMD1030 and TMD0621 are predominantly and selectively expressed in spleen tissue.

The expression patterns of the selectively expressed polynucleotides disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by a tissue.

Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of expressed sequences disclosed herein

5 provides an example of such a tissue expression profile. It can be used as a point of reference to compare and characterize samples. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue, to determine the origin of metastatic cells, to assess the physiological status of a tissue, to determine the effect of a particular treatment regime on a tissue, to evaluate the toxicity of a compound on a tissue of interest, etc.

10 For example, the tissue-selective polynucleotides disclosed herein represent the configuration of genes expressed by a normal tissue. To determine the effect of a toxin on a tissue, a sample of tissue can be obtained prior to toxin exposure ("control") and then at one or more time points after toxin exposure ("experimental"). An array of tissue-selective probes can be used to assess the expression patterns for both the control and experimental

15 samples. As discussed in more detail below, any suitable method can be used. For instance, a DNA microarray can be prepared having a set of tissue-selective genes arranged on to a small surface area in fixed and addressable positions. RNA isolated from samples can be labeled using reverse transcriptase and radioactive nucleotides, hybridized to the array, and then expression levels determined using a detection system. Several kinds of information can

20 be extracted: presence or absence of expression, and the corresponding expression levels. The normal tissue would be expected to express substantially all the genes represented by the tissue-selective probes. The various experimental conditions can be compared to it to determine whether a gene is expressed, and how its levels match up to the normal control.

While the expression profile of the complete gene set represented by the sequences
25 disclosed here may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample.
30 Moreover, because of heterogeneity of the population, as well differences in the particular physiological state of the tissue, a tissue's "normal" expression profile is expected to differ

between samples, albeit in ways that do not change the overall expression pattern. As a result of these individual differences, each gene although expressed selectively in spleen, may not on its own 100% of the time be adequately enough expressed to distinguish said tissue.

Thus, the genes can be used in any of the methods and processes mentioned above and below 5 as a group, or one at a time.

The present invention relates to methods of detecting spleen, lymphoid, and/or reticuloendothelial cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a polynucleotide specific for TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), or a 10 mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically to said gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include SEQ ID NOS 197-204 listed in Table 17, and complements thereto.

15 Detection can also be achieved using binding partners, such as antibodies (e.g., monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting a spleen, lymphoid, and/or reticuloendothelial cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an 20 Fab fragment, a single-chain antibody, an aptamer) specific for a polypeptide coded for by a polypeptide of the present invention, or a mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those 25 exposed to the surface. Detection can be useful for assessing spleen integrity, e.g., when it is suspected that the spleen is damaged and undergoing deterioration. The appearance of polypeptides of the present invention in body fluids, such as blood, can indicate spleen damage, including neoplastic and/or apoptotic changes.

As indicated above, binding partners can be used to deliver agents specifically to the 30 spleen, lymphoid, and/or reticuloendothelial tissues, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to a spleen, lymphoid, and/or

reticuloendothelial cell can comprise, e.g., contacting a spleen, lymphoid, and/or reticuloendothelial cell with an agent coupled to a binding partner specific for a polypeptide coding for TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), whereby said agent is delivered to said cell. Any type of agent can

- 5 be used, including, therapeutic and imaging agents. Contact with the spleen, lymphoid, and/or reticuloendothelial tissue can be achieved in any effective manner, including by administering effective amounts of the agent to a host orally, parenterally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried
- 10 specifically to the target site. Coupling includes, chemical bonding, covalent bonding, noncovalent bonding (where such bonding is sufficient to carry the agent to the target), present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers. Any cell expressing a polypeptide coded for by TMD1030 (XM_166853),
- 15 TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205) can be targeted, including, e.g., reticuloendothelial cells, macrophages, Kupffer cells, lymphocytes, B-lymphocytes, T-lymphocytes, etc.

Antibodies (alone or conjugated to active agents) can be used to ablate spleen and other tissues. For instance, in diseases where splenectomy is indicated (e.g., immune

- 20 thrombocytopenic purpura, autoimmune hemolytic anemia, blood cell disorders, myeloproliferative disorders, tumors, hypersplenism, etc.), antibodies to TMD1030 and TMD0621 can be used to ablate spleen tissue, or block spleen function.

Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body.

- 25 Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintiographic imaging. A reporter agent can be conjugated or associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos, 6,264,917, 6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The
- 30

methods described therein can be used generally to associate a partner with an agent for any desired purpose. See, Bruehlmeier et al., *Nucl. Med. Biol.*, 29:321-327, 2002, for imaging using labeled receptor ligands. Antibodies and other ligands to receptors of the present invention can be used analogously.

- 5 A cell (see above for examples of spleen, lymphoid, and/or reticuloendothelial cell types) can also be modulated in accordance with the present invention, e.g., by methods of modulating a spleen, lymphoid, and/or reticuloendothelial cell, comprising, e.g., contacting said cell with an agent effective to modulate TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), or the biological activity of a polypeptide encoded thereby (e.g., SEQ ID NOS 185-192), or a mammalian homolog thereof, whereby said spleen, lymphoid, and/or reticuloendothelial cell is modulated. Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.
- 10 Any activity or function of the spleen, lymphoid, and/or reticuloendothelial tissues can be modulated, including, e.g., immune modulation (e.g., modulating antigen presentation, antibody production and secretion, humoral and cellular responses, etc.), sequestration and removal of red blood cells, clearance of microorganisms and particular antigens from blood, migration into the marginal zone or other immune and RES compartments, etc.
- 15 The present invention also relates to polypeptide detection methods for assessing spleen, lymphoid, and/or reticuloendothelial tissue function, e.g., methods of assessing spleen, lymphoid, and/or reticuloendothelial function, comprising, detecting a polypeptide coded for by TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), fragments thereof, polymorphisms thereof, in a body fluid,
- 20 whereby the level of said polypeptide in said fluid is a measure of spleen, lymphoid, and/or reticuloendothelial function. spleen, lymphoid, and/or reticuloendothelial function tests are usually performed to determine whether the spleen, lymphoid, and/or reticuloendothelial tissue is functioning normally as a way of diagnosing spleen, lymphoid, and/or reticuloendothelial disease. Various tests are commonly used, including, e.g., ⁹⁹Tc-colloid
- 25 liver-spleen scan, computed tomography, ultrasound scanning of left upper quadrant, MRI, liver enzymes, etc.
- 30

Detection of a polypeptide coded for by TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), provides an additional assessment tool, especially in diseases or disorders, such as splenomegaly, hypersplenism, or ruptured spleen, where said polypeptides can appear in the blood, stool, 5 urine, and other body fluids. As with the other tests, elevated levels of said polypeptide in blood, or other fluids, can indicate impaired spleen, lymphoid, and/or reticuloendothelial function. Values can be determined routinely, as they are for other markers , such as those mentioned above. Detecting can be performed routinely (see below), e.g., using an antibody which is specific for said polypeptide, by RIA, ELISA, or Western blot, etc., in analogy to the 10 tests for enzymes and other proteins in body fluids.

Promoter sequences obtained from genes of the present invention can be utilized to selectively express heterologous genes in cells. Methods of expressing a heterologous polynucleotide in cells, e.g., spleen, lymphoid, and/or reticuloendothelial cells can comprise, e.g., expressing a nucleic acid construct in spleen, lymphoid, and/or reticuloendothelial cells, 15 said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected SEQ ID NOS 205-213. In addition to the cell lines mentioned below, the construct can be expressed in primary cells or in established cell lines.

The genes and polypeptides of the present invention can be used to identify, detect, 20 stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of the spleen, lymphoid, and/or reticuloendothelial tissues mentioned above. The present invention relates to methods of identifying a genetic basis for a disease or disease-susceptibility, comprising, e.g., determining the association of a spleen, lymphoid, and/or reticuloendothelial disease or spleen, lymphoid, and/or reticuloendothelial disease-susceptibility with the gene complex of the present invention, e.g., a nucleotide sequence 25 present in the gene complex at 11q12.2. An association between a spleen, lymphoid, and/or reticuloendothelial disease or disease-susceptibility and nucleotide sequence includes, e.g., establishing (or finding) a correlation (or relationship) between a DNA marker (e.g., gene, VNTR, polymorphism, EST, etc.) and a particular disease state. Once a relationship is identified, the DNA marker can be utilized in diagnostic tests and as a drug target.

Any region of the gene can be used as a source of the DNA marker, exons, introns,

intergenic regions, or any DNA from the gene cluster of the present invention at chromosomal region 11q12.2, etc.

Human linkage maps can be constructed to establish a relationship between a gene and a spleen, lymphoid, and/or reticuloendothelial disease or condition. Typically, within the region, linkage and map distance between the markers is then established, and then linkage is established between phenotype and the various individual molecular markers.

5 Maps can be produced for an individual family, selected populations, patient populations, etc.

In general, these methods involve identifying a marker associated with the disease (e.g.,

10 identifying a polymorphism in a family which is linked to the disease) and then analyzing the surrounding DNA to identify the gene responsible for the phenotype.

The present invention also relates to methods of expressing a polynucleotide in spleen, lymphoid, and/or reticuloendothelial tissue, comprising, e.g., inserting a polynucleotide, which is operably linked to an expression control sequence, into the spleen, 15 lymphoid, and/or reticuloendothelial gene complex at chromosomal location 11q12.2 of a target cell, and growing said cell under conditions effective to express said polynucleotide.

The polynucleotide of interest can be inserted into the target chromosomal region by any suitable method, including, e.g., by gene targeting methods, such as homologous recombination, or by random insertion methods where transformed cells are subsequently

20 screened for insertion into the desired chromosomal site. Chromosome engineering methods are discussed in more detail below, e.g., in the section on transgenic animals. By the phrase "spleen, lymphoid, and/or reticuloendothelial gene complex," it is meant the region of the chromosome in which the cluster of genes, e.g., TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), and TMD0621 (XM_166205), of the present

25 invention are located. Inserting an expressible polynucleotide (e.g., a polynucleotide operably linked to a promoter sequence) into this region confers the tissue expression selectivity which is characteristic of the gene cluster. Any polynucleotide of interest can be inserted into the chromosomal region, including, e.g., polynucleotides encoding polypeptides, antisense polynucleotides, etc.

30 A cell comprising a polynucleotide inserted into the target chromosomal location can be utilized in vitro or in vivo, e.g., in a transgenic animal. The cell is grown under conditions

which are suitable to achieve polynucleotide expression. These conditions depend upon the cell's environment, e.g., tissue culture cell, or in the form of a transgenic animal.

Pancreas membrane protein genes

- 5 The present invention relates to all facets of pancreas membrane protein genes, polypeptides encoded by them, antibodies and specific binding partners thereto, and their applications to research, diagnosis, drug discovery, therapy, clinical medicine, forensic science and medicine, etc. The polynucleotides and polypeptides are useful in variety of ways, including, but not limited to, as molecular markers, as drug targets, and for detecting,
- 10 diagnosing, staging, monitoring, prognosticating, preventing or treating, determining predisposition to, etc., diseases and conditions, such as pancreatic cancer, diabetes, pancreatitis, and other disorders especially relating to the pancreas and the functions it performs. The identification of specific genes, and groups of genes, expressed in pathways physiologically relevant to pancreas tissue permits the definition of functional and disease
- 15 pathways, and the delineation of targets in these pathways which are useful in diagnostic, therapeutic, and clinical applications. The present invention also relates to methods of using the polynucleotides and related products (proteins, antibodies, etc.) in business and computer-related methods, e.g., advertising, displaying, offering, selling, etc., such products for sale, commercial use, licensing, etc.
- 20 The function, structure, and diseases of the pancreas were described previously. The polynucleotides, polypeptides, and ligands thereto, of the present invention can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions of pancreas. These include, but are not limited to, e.g., acute and chronic pancreatitis, pancreatic abscess, pancreatic pseudocyst, nonalcoholic pancreatitis, alcoholic
- 25 pancreatitis, classic acute hemorrhagic pancreatitis, chronic calcifying pancreatitis, familial hereditary pancreatitis, carcinomas of the pancreas, primary (idiopathic) diabetes (e.g., Type I (insulin dependent diabetes mellitus, IDDM) [insulin deficiency, beta cell depletion], Type II (non-insulin dependent diabetes mellitus, NIDDM) [insulin resistance, relative insulin deficiency, mild beta cell depletion]), nonobese NIDDM, obese NIDDM, maturity-onset
- 30 diabetes of the young (MODY), islet cell tumors, diffuse hyperplasia of the islets of Langerhans, benign adenomas, malignant islet tumors, hyperfunction of the islets of Langerhans, hyperinsulinism and hypoglycemia, Zollinger-Ellison syndrome, beta cell

tumors (insulinoma), alpha cell tumors (glucagonoma), delta cell tumors (somatostatinoma), vipoma (diarrheogenic islet cell tumor), pancreatic cancers, pancreatic carcinoid tumors, multihormonal tumors, multiple endocrine neoplasia (MEN), MEN I (Wermer syndrome), MEN II (Sipple syndrome), MEN III or IIb, pancreatic endocrine tumors, etc.

5 For example, five different pancreatic tumor samples were examined (Nos. 1, 2, 3, 4, and 5). TMD0639 was up-regulated in about 1/5 pancreatic cancers (No. 4), TMD0645 was up-regulated in about 3/5 pancreatic cancers (Nos. 2, 3, and 5), and TMD1127 was up-regulated in about 2/5 pancreatic cancers (Nos. 1 and 4). These results indicate that the probes can be used in combination in order to maximize the detection of different types of
10 pancreatic cancers and tumors. Thus, a sample from a patient can be assessed for expression of both TMD0645 and TMD1127 to increase the probability that the pancreas cancer will be detected.

In view of their selectivity and display on the cell surface, the membrane proteins of the present invention are useful targets for histological, diagnostic, and therapeutic
15 applications relating to the cells (e.g., pancreatic progenitor, exocrine, endocrine, acinar, islet, alpha, beta, delta, F, D1, enterochromaffin, etc.) in which they are expressed. Antibodies and other protein binding partners (e.g., ligands, aptamers, small peptides, etc.) can be used to selectively target agents to a tissue for any purpose, included, but not limited to, imaging, therapeutic, diagnostic, drug delivery, gene therapy, etc. For example, binding partners, such
20 as antibodies, can be used to treat carcinomas in analogy to how c-erbB-2 antibodies are used to breast cancer. They can also be used to detect metastatic cells in biopsies and other tissue samples. The genes and polypeptides encoded thereby can also be used in tissue engineering to identify tissues as they appear during the differentiation process, to target tissues, to modulate tissue growth (e.g., from starting stem cell populations), etc. Useful antibodies or
25 other binding partners include those that are specific for parts of the polypeptide which are exposed extracellularly as indicated in Table 21. Any of the methods described above and below can be accomplished in vivo, in vitro, or ex vivo.

When expression is described as being "predominantly" in a given tissue, this indicates that the gene's mRNAs levels are highest in this tissue as compared to the other
30 tissues in which it was measured. Expression can also be "selective," where expression is observed. By the phrase "selectively expressed," it is meant that a nucleic acid molecule

comprising the defined sequence of nucleotides, when produced as a transcript, is characteristic of the tissue or cell-type in which it is made. This can mean that the transcript is expressed only in that tissue and in no other tissue-type, or it can mean that the transcript is expressed preferentially, differentially, and more abundantly (e.g., at least 5-fold, 10-fold, etc., or more) in that tissue when compared to other tissue-types.

Table 20 is a summary of the genes of the present invention which are expressed selectively and/or predominantly in pancreas tissue. Fig. 12 is an illustration of these expression patterns. Each gene is associated with a Clone ID and Accession Number ("ACCN"). The Clone ID is an arbitrary identification number for the clone, and the accession number is the number by which it is listed in GenBank. Although specific sequences are disclosed herein, and listed in GenBank by an accession number), the present invention includes all forms of the gene, including polymorphisms, allelic variations, SNPs, splice variants, and any full-length versions when the disclosed or Genbank version is partial. For convenience, these genes, and their homologs in other species, are referred to throughout the disclosure in shorthand as "the genes of Table 20," "a gene of Table 20," "polynucleotides of Table 20," "polypeptides of Table 20," etc., because Table 20 contains a listing of the genes by accession number and clone ID.

The expression patterns of the selectively and/or predominantly expressed polynucleotides disclosed herein can be described as a "fingerprint" in that they are a distinctive pattern displayed by pancreas tissue. Just as with a fingerprint, an expression pattern can be used as a unique identifier to characterize the status of a tissue sample. The list of expressed sequences disclosed herein provides an example of such a tissue expression profile. It can be used as a point of reference to compare and characterize samples. Tissue fingerprints can be used in many ways, e.g., to classify an unknown tissue, to determine the origin of metastatic cells, to assess the physiological status of a tissue, to determine the effect of a particular treatment regime on a tissue, to evaluate the toxicity of a compound on a tissue of interest, etc.

For example, the pancreas-selective polynucleotides disclosed herein represent the configuration of genes expressed by a normal pancreas tissue. To determine the effect of a toxin on a tissue, a sample of tissue can be obtained prior to toxin exposure ("control") and then at one or more time points after toxin exposure ("experimental"). An array of pancreas-

selective probes can be used to assess the expression patterns for both the control and experimental samples. As discussed in more detail below, any suitable method can be used. For instance, a DNA microarray can be prepared having a set of pancreas-selective genes arranged on to a small surface area in fixed and addressable positions. RNA isolated from 5 samples can be labeled using reverse transcriptase and radioactive nucleotides, hybridized to the array, and then expression levels determined using a detection system. Several kinds of information can be extracted: presence or absence of expression, and the corresponding expression levels. The normal tissue would be expected to express substantially all the genes represented by the tissue-selective probes. The various experimental conditions can be 10 compared to it to determine whether a gene is expressed, and how its levels match up to the normal control.

While the expression profile of the complete gene set represented by the sequences disclosed here may be most informative, a fingerprint containing expression information from less than the full collection can be useful, as well. In the same way that an incomplete 15 fingerprint may contain enough of the pattern of whorls, arches, loops, and ridges, to identify the individual, a cell expression fingerprint containing less than the full complement may be adequate to provide useful and unique identifying and other information about the sample. Moreover, because of heterogeneity of the population, as well differences in the particular 20 physiological state of the tissue, a tissue's "normal" expression profile is expected to differ between samples, albeit in ways that do not change the overall expression pattern. As a result, a complete match with a particular tissue expression profile, as shown herein, is not necessary.

The present invention relates to methods of detecting pancreas cells, comprising one or more of the following steps, e.g., contacting a sample comprising cells with a 25 polynucleotide specific for a gene of Table 20, or a mammalian homolog thereof, under conditions effective for said polynucleotide to hybridize specifically to said gene, and detecting specific hybridization. Detecting can be accomplished by any suitable method and technology, including, e.g., any of those mentioned and discussed below, such as Northern blot and PCR. Specific polynucleotides include the primer sequences shown in Table 23, and 30 complements thereto.

Detection can also be achieved using binding partners, such as antibodies (e.g.,

monoclonal or polyclonal antibodies) that specifically recognize polypeptides coded for by genes of the present invention. Thus, the present invention relates to methods of detecting a pancreas cell, comprising, one or more the following steps, e.g. contacting a sample comprising cells with a binding partner (e.g. an antibody, an Fab fragment, a single-chain

5 antibody, an aptamer) specific for a polypeptide coded for by a polypeptide of Table 20, or a mammalian homolog thereof, under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding. Protein binding assays can be accomplished routinely, e.g., using immunocytochemistry, ELISA format, Western blots, etc. Useful epitopes include those exposed to the surface.

10 As indicated above, binding partners can be used to deliver agents specifically to the pancreas, e.g., for diagnostic, therapeutic, and prognostic purposes. Methods of delivering an agent to a pancreas cell can comprise, e.g., contacting a pancreas cell with an agent coupled to a binding partner specific for a polypeptide coding for a gene of Table 20, whereby said agent is delivered to said cell. Any type of agent can be used, including, therapeutic and
15 imaging agents. Contact with the pancreas can be achieved in any effective manner, including by administering effective amounts of the agent to a host orally, parentally, locally, systemically, intravenously, etc. The phrase "an agent coupled to binding partner" indicates that the agent is associated with the binding partner in such a manner that it can be carried specifically to the target site. Coupling includes, chemical bonding, covalent bonding,
20 noncovalent bonding (where such bonding is sufficient to carry the agent to the target), present in a liposome or in a lipid membrane, associated with a carrier, such as a polymeric carrier, etc. The agent can be directly linked to the binding partner, or via chemical linkers or spacers. Any cell expressing a polypeptide coded for by a gene of Table 20 can be targeted, including, e.g., pancreatic progenitor, exocrine, endocrine, secretory, acinar, islet, alpha, beta,
25 delta, F, D1, enterochromaffin, etc.

Imaging of specific organs can be facilitated using tissue selective antibodies and other binding partners that selectively target contrast agents to a specific site in the body. Various imaging techniques have been used in this context, including, e.g., X-ray, CT, CAT, MRI, ultrasound, PET, SPECT, and scintographic. A reporter agent can be conjugated or
30 associated routinely with a binding partner. Ultrasound contrast agents combined with binding partners, such as antibodies, are described in, e.g., U.S. Pat. Nos, 6,264,917,

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6,254,852, 6,245,318, and 6,139,819. MRI contrast agents, such as metal chelators, radionucleotides, paramagnetic ions, etc., combined with selective targeting agents are also described in the literature, e.g., in U.S. Pat. Nos. 6,280,706 and 6,221,334. The methods described therein can be used generally to associate a partner with an agent for any desired purpose. See, Bruehlmeier et al., *Nucl. Med. Biol.*, 29:321-327, 2002, for imaging pancreas using labeled receptor ligands. Antibodies and other ligands to receptors of the present invention can be used analogously.

A pancreas cell (see above for examples of pancreas cell types) can also be modulated in accordance with the present invention, e.g., by methods of modulating a pancreas cell, comprising, e.g., contacting said cell with an agent effective to modulate a gene of Table 20, or the biological activity of a polypeptide encoded thereby (e.g., SEQ ID NO 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, and 255), or a mammalian homolog thereof, whereby said pancreas cell is modulated.

Modulation as used throughout includes, e.g., stimulating, increasing, agonizing, activating, amplifying, blocking, inhibiting, reducing, antagonizing, preventing, decreasing, diminishing, etc.

An activity or function of the pancreas cell can be modulated, including, e.g., regulation of blood sugar, modulation of all aspects of the various secreted polypeptides (hormones, enzymes, etc.) produced by the pancreas, ligand-binding, exocytosis, amylase (and any of the other 20 or so digestive enzymes produced by the pancreas) secretion, autocrine responses, apoptosis (e.g., in the survival of beta-islet cells), etc.

The present invention also relates to polypeptide detection methods for assessing pancreas function, e.g., methods of assessing pancreas function, comprising, detecting a polypeptide coded for by a gene of Table 20, fragments thereof, polymorphisms thereof, in a body fluid, whereby the level of said polypeptide in said fluid is a measure of pancreas function. Pancreas function tests are usually performed to determine whether the pancreas is functioning normally as a way of diagnosing pancreas disease. Various tests are commonly used, including, e.g., assays for the presence of pancreatic enzymes in body fluids (e.g., amylase, serum lipase, serum trypsin-like immunoactivity), studies of pancreatic structure (e.g., using x-ray, sonography, CT-scan, angiography, endoscopic retrograde cholangiopancreatography), and tests for pancreatic function (e.g., secretin-pancreozymin

(CCK) test, Lundh meal test, Bz-Ty-PABA test, chymotrypsin in feces, etc). Detection of a polypeptide coded for by a gene of Table 20 provides an additional assessment tool, especially in diseases such as pancreatitis and pancreatic cancer where pancreatic markers can appear in the blood, stool, urine, and other body fluids. As with the other tests, elevated levels of said polypeptide in blood, or other fluids, can indicate impaired pancreas function. Values can be determined routinely, as they are for other markers, such as those mentioned above. Detecting can be performed routinely (see below), e.g., using an antibody which is specific for said polypeptide, by RIA, ELISA, or Western blot, etc., in analogy to the tests for pancreatic enzymes in body fluids.

- 10 Promoter sequences obtained from genes of the present invention can be utilized to selectively express heterologous genes in pancreas cells. Methods of expressing a heterologous polynucleotide in pancreas cells can comprise, e.g., expressing a nucleic acid construct in pancreas cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected SEQ ID NO
15 258, 261, 262, 265-267, 270-272, 275, 278, 279, 282-284, 287, 290-293, 296, 297, 303, 306, 309-314, 317-320, 323-326, 329, 332-333, 336-338, 341, and 344 as shown in Table 23. In addition to the cell lines mentioned below, the construct can be expressed in primary cells or in established cell lines.

- The genes and polypeptides of Table 20 can be used to identify, detect, stage,
20 determine the presence of, prognosticate, treat, study, etc., diseases and conditions of the pancreas as mentioned above. The present invention relates to methods of identifying a pancreatic disease or pancreatic disease-susceptibility, comprising, e.g., determining the association of a pancreatic disease or pancreatic disease-susceptibility with a nucleotide sequence present within the pancreatic gene complex. An association between a pancreas
25 disease or disease-susceptibility and nucleotide sequence includes, e.g., establishing (or finding) a correlation (or relationship) between a DNA marker (e.g., gene, VNTR, polymorphism, EST, etc.) and a particular disease state. Once a relationship is identified, the DNA marker can be utilized in diagnostic tests and as a drug target.

- Human linkage maps can be constructed to establish a relationship between the
30 cytogenetic locus as shown in Table 22 and a pancreatic disease or condition. Typically, polymorphic molecular markers (e.g., STRP's, SNP's, RFLP's, VNTR's) are identified

within the region, linkage and map distance between the markers is then established, and then linkage is established between phenotype and the various individual molecular markers. Maps can be produced individual family, selected populations, patient populations, etc. In general, these methods involve identifying a marker associated with the disease (e.g., 5 identifying a polymorphism in a family which is linked to the disease) and then analyzing the surrounding DNA to identify the gene responsible for the phenotype.

Nucleic acids

A mammalian polynucleotide, or fragment thereof, of the present invention is a 10 polynucleotide having a nucleotide sequence obtainable from a natural source. When the species name is used, e.g., a human, it indicates that the polynucleotide or polypeptide is obtainable from a natural source. It therefore includes naturally-occurring normal, naturally- occurring mutant, and naturally-occurring polymorphic alleles (e.g., SNPs), differentially- spliced transcripts, splice-variants, etc. By the term "naturally-occurring," it is meant that the 15 polynucleotide is obtainable from a natural source, e.g., animal tissue and cells, body fluids, tissue culture cells, forensic samples. Natural sources include, e.g., living cells obtained from tissues and whole organisms, tumors, cultured cell lines, including primary and immortalized cell lines. Naturally-occurring mutations can include deletions (e.g., a truncated amino- or carboxy-terminus), substitutions, inversions, or additions of nucleotide sequence. These 20 genes can be detected and isolated by polynucleotide hybridization according to methods which one skilled in the art would know, e.g., as discussed below.

A polynucleotide according to the present invention can be obtained from a variety of different sources. It can be obtained from DNA or RNA, such as polyadenylated mRNA or total RNA, e.g., isolated from tissues, cells, or whole organism. The polynucleotide can be 25 obtained directly from DNA or RNA, from a cDNA library, from a genomic library, etc. The polynucleotide can be obtained from a cell or tissue (e.g., from an embryonic or adult tissues) at a particular stage of development, having a desired genotype, phenotype, disease status, etc.

The polynucleotides described herein can be partial sequences that correspond to full-length, naturally-occurring transcripts. The present invention includes, as well, full-length 30 polynucleotides that comprise these partial sequences, e.g., genomic DNAs and polynucleotides comprising a start and stop codon, a start codon and a polyA tail, a

transcription start and a polyA tail, etc. These sequences can be obtained by any suitable method, e.g., using a partial sequence as a probe to select a full-length cDNA from a library containing full-length inserts. A polynucleotide which "codes without interruption" refers to a polynucleotide having a continuous open reading frame ("ORF") as compared to an ORF
5 which is interrupted by introns or other noncoding sequences.

Polynucleotides and polypeptides can be excluded as compositions from the present invention if, e.g., listed in a publicly available databases on the day this application was filed and/or disclosed in a patent application having an earlier filing or priority date than this application and/or conceived and/or reduced to practice earlier than a polynucleotide in this
10 application.

As described herein, the phrase "an isolated polynucleotide which is SEQ ID NO," or "an isolated polynucleotide which is selected from SEQ ID NO," refers to an isolated nucleic acid molecule from which the recited sequence was derived (e.g., a cDNA derived from mRNA; cDNA derived from genomic DNA). Because of sequencing errors, typographical
15 errors, etc., the actual naturally-occurring sequence may differ from a SEQ ID listed herein. Thus, the phrase indicates the specific molecule from which the sequence was derived, rather than a molecule having that exact recited nucleotide sequence, analogously to how a culture depository number refers to a specific cloned fragment in a cryotube.

As explained in more detail below, a polynucleotide sequence of the invention can
20 contain the complete sequence as shown herein, degenerate sequences thereof, anti-sense, muteins thereof, genes comprising said sequences, full-length cDNAs comprising said sequences, complete genomic sequences, fragments thereof, homologs, primers, nucleic acid molecules which hybridize thereto, derivatives thereof, etc.

25 Genomic

The present invention also relates genomic DNA from which the polynucleotides of the present invention can be derived. A genomic DNA coding for a human, mouse, or other mammalian polynucleotide, can be obtained routinely, for example, by screening a genomic library (e.g., a YAC library) with a polynucleotide of the present invention, or by searching
30 nucleotide databases, such as GenBank and EMBL, for matches. Promoter and other regulatory regions (including both 5' and 3' regions, as well introns) can be identified

upstream or downstream of coding and expressed RNAs, and assayed routinely for activity, e.g., by joining to a reporter gene (e.g., CAT, GFP, alkaline phosphatase, luciferase, galatosidase). A promoter obtained from a tissue selective gene can be used, e.g., in gene therapy to obtain tissue-specific expression of a heterologous gene (e.g., coding for a therapeutic product or cytotoxin). 5' and 3' sequences (including, UTRs and introns) can be used to modulate or regulate stability, transcription, and translation of nucleic acids, including the sequence to which is attached in nature, as well as heterologous nucleic acids.

Constructs

A polynucleotide of the present invention can comprise additional polynucleotide sequences, e.g., sequences to enhance expression, detection, uptake, cataloging, tagging, etc. A polynucleotide can include only coding sequence; a coding sequence and additional non-naturally occurring or heterologous coding sequence (e.g., sequences coding for leader, signal, secretory, targeting, enzymatic, fluorescent, antibiotic resistance, and other functional or diagnostic peptides); coding sequences and non-coding sequences, e.g., untranslated sequences at either a 5' or 3' end, or dispersed in the coding sequence, e.g., introns.

A polynucleotide according to the present invention also can comprise an expression control sequence operably linked to a polynucleotide as described above. The phrase "expression control sequence" means a polynucleotide sequence that regulates expression of a polypeptide coded for by a polynucleotide to which it is functionally ("operably") linked. Expression can be regulated at the level of the mRNA or polypeptide. Thus, the expression control sequence includes mRNA-related elements and protein-related elements. Such elements include promoters, enhancers (viral or cellular), ribosome binding sequences, transcriptional terminators, etc. An expression control sequence is operably linked to a nucleotide coding sequence when the expression control sequence is positioned in such a manner to effect or achieve expression of the coding sequence. For example, when a promoter is operably linked 5' to a coding sequence, expression of the coding sequence is driven by the promoter. Expression control sequences can include an initiation codon and additional nucleotides to place a partial nucleotide sequence of the present invention in-frame in order to produce a polypeptide (e.g., pET vectors from Promega have been designed to permit a molecule to be inserted into all three reading frames to identify the one that results

in polypeptide expression). Expression control sequences can be heterologous or endogenous to the normal gene.

A polynucleotide of the present invention can also comprise nucleic acid vector sequences, e.g., for cloning, expression, amplification, selection, etc. Any effective vector 5 can be used. A vector is, e.g., a polynucleotide molecule which can replicate autonomously in a host cell, e.g., containing an origin of replication. Vectors can be useful to perform manipulations, to propagate, and/or obtain large quantities of the recombinant molecule in a desired host. A skilled worker can select a vector depending on the purpose desired, e.g., to propagate the recombinant molecule in bacteria, yeast, insect, or mammalian cells. The 10 following vectors are provided by way of example. Bacterial: pQE70, pQE60, pQE-9 (Qiagen), pBS, pD10, Phagescript, phiX174, pBK Phagemid, pNH8A, pNH16a, pNH18Z, pNH46A (Stratagene); Bluescript KS+II (Stratagene); ptrc99a, pKK223-3, pKK233-3, pDR54 0, pRITS (Pharmacia). Eukaryotic: PWLNEO, pSV2CAT, pOG44, pXT1, pSG (Stratagene), pSVK3, PBPV, PMSG, pSVL (Pharmacia), pCR2.1/TOPO, pCRII/TOPO, 15 pCR4/TOPO, pTrcHisB, pCMV6-XL4, etc. However, any other vector, e.g., plasmids, viruses, or parts thereof, may be used as long as they are replicable and viable in the desired host. The vector can also comprise sequences which enable it to replicate in the host whose genome is to be modified.

20 Hybridization

Polynucleotide hybridization, as discussed in more detail below, is useful in a variety of applications, including, in gene detection methods, for identifying mutations, for making mutations, to identify homologs in the same and different species, to identify related members of the same gene family, in diagnostic and prognostic assays, in therapeutic 25 applications (e.g., where an antisense polynucleotide is used to inhibit expression), etc.

The ability of two single-stranded polynucleotide preparations to hybridize together is a measure of their nucleotide sequence complementarity, e.g., base-pairing between nucleotides, such as A-T, G-C, etc. The invention thus also relates to polynucleotides, and their complements, which hybridize to a polynucleotide comprising a nucleotide sequence as 30 set forth herein and genomic sequences thereof. A nucleotide sequence hybridizing to the latter sequence will have a complementary polynucleotide strand, or act as a template for one

in the presence of a polymerase (i.e., an appropriate polynucleotide synthesizing enzyme). The present invention includes both strands of polynucleotide, e.g., a sense strand and an anti-sense strand.

Hybridization conditions can be chosen to select polynucleotides which have a desired amount of nucleotide complementarity with the nucleotide sequences set forth in herein and genomic sequences thereof. A polynucleotide capable of hybridizing to such sequence, preferably, possesses, e.g., about 70%, 75%, 80%, 85%, 87%, 90%, 92%, 95%, 97%, 99%, or 100% complementarity, between the sequences. The present invention particularly relates to polynucleotide sequences which hybridize to the nucleotide sequences set forth in the attached sequence disclosure or genomic sequences thereof, under low or high stringency conditions. These conditions can be used, e.g., to select corresponding homologs in non-human species.

Polynucleotides which hybridize to polynucleotides of the present invention can be selected in various ways. Filter-type blots (i.e., matrices containing polynucleotide, such as nitrocellulose), glass chips, and other matrices and substrates comprising polynucleotides (short or long) of interest, can be incubated in a prehybridization solution (e.g., 6X SSC, 0.5% SDS, 100 µg/ml denatured salmon sperm DNA, 5X Denhardt's solution, and 50% formamide), at 22-68°C, overnight, and then hybridized with a detectable polynucleotide probe under conditions appropriate to achieve the desired stringency. In general, when high homology or sequence identity is desired, a high temperature can be used (e.g., 65 °C). As the homology drops, lower washing temperatures are used. For salt concentrations, the lower the salt concentration, the higher the stringency. The length of the probe is another consideration. Very short probes (e.g., less than 100 base pairs) are washed at lower temperatures, even if the homology is high. With short probes, formamide can be omitted.

See, e.g., *Current Protocols in Molecular Biology*, Chapter 6, Screening of Recombinant Libraries; Sambrook et al., *Molecular Cloning*, 1989, Chapter 9.

For instance, high stringency conditions can be achieved by incubating the blot overnight (e.g., at least 12 hours) with a polynucleotide probe in a hybridization solution containing, e.g., about 5X SSC, 0.1-0.5% SDS, 100 µg/ml denatured salmon sperm DNA and 50% formamide, at 42°C, or hybridizing at 42°C in 5X SSPE, 0.1-0.5% SDS, and 50%

formamide, 100 µg/ml denatured salmon sperm DNA, and washing at 65°C in 0.1% SSC and 0.1% SDS.

Blots can be washed at high stringency conditions that allow, e.g., for less than 5% bp mismatch (e.g., wash twice in 0.1% SSC and 0.1% SDS for 30 min at 65°C), i.e.,

5. selecting sequences having 95% or greater sequence identity.

Other non-limiting examples of high stringency conditions includes a final wash at 65°C in aqueous buffer containing 30 mM NaCl and 0.5% SDS. Another example of high stringent conditions is hybridization in 7% SDS, 0.5 M NaPO₄, pH 7, 1 mM EDTA at 50°C, e.g., overnight, followed by one or more washes with a 1% SDS solution at 42°C.

- 10 Whereas high stringency washes can allow for, e.g., less than 10%, less than 5% mismatch, etc., reduced or low stringency conditions can permit up to 20% nucleotide mismatch.

Hybridization at low stringency can be accomplished as above, but using lower formamide conditions, lower temperatures and/or lower salt concentrations, as well as longer periods of incubation time.

- 15 Hybridization can also be based on a calculation of melting temperature (T_m) of the hybrid formed between the probe and its target, as described in Sambrook et al.. Generally, the temperature T_m at which a short oligonucleotide (containing 18 nucleotides or fewer) will melt from its target sequence is given by the following equation: T_m = (number of A's and T's) x 2°C + (number of C's and G's) x 4°C. For longer molecules, T_m = 81.5 + 16.6
20 log₁₀[Na⁺] + 0.41(%GC) - 600/N where [Na⁺] is the molar concentration of sodium ions, %GC is the percentage of GC base pairs in the probe, and N is the length. Hybridization can be carried out at several degrees below this temperature to ensure that the probe and target can hybridize. Mismatches can be allowed for by lowering the temperature even further.

- Stringent conditions can be selected to isolate sequences, and their complements,
25 which have, e.g., at least about 90%, 95%, or 97%, nucleotide complementarity between the probe (e.g., a short polynucleotide of the sequences disclosed herein or genomic sequences thereof) and a target polynucleotide.

- Other homologs of polynucleotides of the present invention can be obtained from mammalian and non-mammalian sources according to various methods. For example,
30 hybridization with a polynucleotide can be employed to select homologs, e.g., as described in Sambrook et al., *Molecular Cloning*, Chapter 11, 1989. Such homologs can have varying

amounts of nucleotide and amino acid sequence identity and similarity to such polynucleotides of the present invention. Mammalian organisms include, e.g., mice, rats, monkeys, pigs, cows, etc. Non-mammalian organisms include, e.g., vertebrates, invertebrates, zebra fish, chicken, Drosophila, C. elegans, Xenopus, yeast such as S. pombe, 5 S. cerevisiae, roundworms, prokaryotes, plants, Arabidopsis, artemia, viruses, etc. The degree of nucleotide sequence identity between human and mouse can be about, e.g. 70% or more, 85% or more for open reading frames, etc.

Alignment

- 10 Alignments can be accomplished by using any effective algorithm. For pairwise alignments of DNA sequences, the methods described by Wilbur-Lipman (e.g., Wilbur and Lipman, *Proc. Natl. Acad. Sci.*, 80:726-730, 1983) or Martinez/Needleman-Wunsch (e.g., Martinez, *Nucleic Acid Res.*, 11:4629-4634, 1983) can be used. For instance, if the Martinez/Needleman-Wunsch DNA alignment is applied, the minimum match can be set at 15 9, gap penalty at 1.10, and gap length penalty at 0.33. The results can be calculated as a similarity index, equal to the sum of the matching residues divided by the sum of all residues and gap characters, and then multiplied by 100 to express as a percent. Similarity index for related genes at the nucleotide level in accordance with the present invention can be greater than 70%, 80%, 85%, 90%, 95%, 99%, or more. Pairs of protein sequences can be aligned 20 by the Lipman-Pearson method (e.g., Lipman and Pearson, *Science*, 227:1435-1441, 1985) with k-tuple set at 2, gap penalty set at 4, and gap length penalty set at 12. Results can be expressed as percent similarity index, where related genes at the amino acid level in accordance with the present invention can be greater than 65%, 70%, 75%, 80%, 85%, 90%, 95%, 99%, or more. Various commercial and free sources of alignment programs are 25 available, e.g., MegAlign by DNA Star, BLAST (National Center for Biotechnology Information), BCM (Baylor College of Medicine) Launcher, etc. BLAST can be used to calculate amino acid sequence identity, amino acid sequence homology, and nucleotide sequence identity. These calculations can be made along the entire length of each of the target sequences which are to be compared.
- 30 After two sequences have been aligned, a "percent sequence identity" can be determined. For these purposes, it is convenient to refer to a Reference Sequence and a

Compared Sequence, where the Compared Sequence is *compared* to the Reference Sequence.

Percent sequence identity can be determined according to the following formula: Percent

Identity = 100 [1-(C/R)], wherein C is the number of differences between the Reference Sequence and the Compared Sequence over the length of alignment between the Reference

- 5 Sequence and the Compared Sequence where (i) each base or amino acid in the Reference Sequence that does not have a corresponding aligned base or amino acid in the Compared Sequence, (ii) each gap in the Reference Sequence, (iii) each aligned base or amino acid in the Reference Sequence that is different from an aligned base or amino acid in the Compared Sequence, constitutes a difference; and R is the number of bases or amino acids in the
- 10 Reference Sequence over the length of the alignment with the Compared Sequence with any gap created in the Reference Sequence also being counted as a base or amino acid.

Percent sequence identity can also be determined by other conventional methods, e.g., as described in Altschul et al., *Bull. Math. Bio.* 48: 603-616, 1986 and Henikoff and Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915-10919, 1992.

15

Specific polynucleotide probes

A polynucleotide of the present invention can comprise any continuous nucleotide sequence described herein, sequences which share sequence identity thereto, or complements thereof. The term "probe" refers to any substance that can be used to detect, identify, isolate,

20 etc., another substance. A polynucleotide probe is comprised of nucleic acid can be used to detect, identify, etc., other nucleic acids, such as DNA and RNA.

These polynucleotides can be of any desired size that is effective to achieve the specificity desired. For example, a probe can be from about 7 or 8 nucleotides to several thousand nucleotides, depending upon its use and purpose. For instance, a probe used as a

- 25 primer PCR can be shorter than a probe used in an ordered array of polynucleotide probes. Probe sizes vary, and the invention is not limited in any way by their size, e.g., probes can be from about 7-2000 nucleotides, 7-1000, 8-700, 8-600, 8-500, 8-400, 8-300, 8-150, 8-100, 8-75, 7-50, 10-25, 14-16, at least about 8, at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or more, etc. The polynucleotides can have non-naturally-occurring
- 30 nucleotides, e.g., inosine, AZT, 3TC, etc. The polynucleotides can have 100% sequence identity or complementarity to a sequence disclosed herein, or it can have mismatches or

nucleotide substitutions, e.g., 1, 2, 3, 4, or 5 substitutions. The probes can be single-stranded or double-stranded.

In accordance with the present invention, a polynucleotide can be present in a kit, where the kit includes, e.g., one or more polynucleotides, a desired buffer (e.g., phosphate, tris, etc.), detection compositions, RNA or cDNA from different tissues to be used as controls, libraries, etc. The polynucleotide can be labeled or unlabeled, with radioactive or non-radioactive labels as known in the art. Kits can comprise one or more pairs of polynucleotides for amplifying nucleic acids specific for tissue selective genes, e.g., comprising a forward and reverse primer effective in PCR. These include both sense and anti-sense orientations. For instance, in PCR-based methods (such as RT-PCR), a pair of primers are typically used, one having a sense sequence and the other having an antisense sequence.

Another aspect of the present invention is a nucleotide sequence that is specific to, or for, a selective polynucleotide. The phrases "specific for" or "specific to" a polynucleotide have a functional meaning that the polynucleotide can be used to identify the presence of one or more target genes in a sample and distinguish them from non-target genes. It is specific in the sense that it can be used to detect polynucleotides above background noise ("non-specific binding"). A specific sequence is a defined order of nucleotides (or amino acid sequences, if it is a polypeptide sequence) which occurs in the polynucleotide, e.g., in the nucleotide sequences of the present invention, and which is characteristic of that target sequence, and substantially no non-target sequences. A probe or mixture of probes can comprise a sequence or sequences that are specific to a plurality of target sequences, e.g., where the sequence is a consensus sequence, a functional domain, etc., e.g., capable of recognizing a family of related genes. Such sequences can be used as probes in any of the methods described herein or incorporated by reference. Both sense and antisense nucleotide sequences are included. A specific polynucleotide according to the present invention can be determined routinely.

A polynucleotide comprising a specific sequence can be used as a hybridization probe to identify the presence of, e.g., human or mouse polynucleotide, in a sample comprising a mixture of polynucleotides, e.g., on a Northern blot. Hybridization can be performed under high stringent conditions (see, above) to select polynucleotides (and their complements which

can contain the coding sequence) having at least 90%, 95%, 99%, etc., identity (i.e., complementarity) to the probe, but less stringent conditions can also be used. A specific polynucleotide sequence can also be fused in-frame, at either its 5' or 3' end, to various nucleotide sequences as mentioned throughout the patent, including coding sequences for enzymes, detectable markers, GFP, etc, expression control sequences, etc.

A polynucleotide probe, especially one that is specific to a polynucleotide of the present invention, can be used in gene detection and hybridization methods as already described. In one embodiment, a specific polynucleotide probe can be used to detect whether a particular tissue or cell-type is present in a target sample. To carry out such a method, a selective polynucleotide can be chosen which is characteristic of the desired target tissue. Such polynucleotide is preferably chosen so that it is expressed or displayed in the target tissue, but not in other tissues which are present in the sample. For instance, if detection of pancreas, or kidney, it may not matter whether the selective polynucleotide is expressed in other tissues, as long as it is not expressed in cells normally present in blood, e.g., peripheral blood mononuclear cells. Starting from the selective polynucleotide, a specific polynucleotide probe can be designed which hybridizes (if hybridization is the basis of the assay) under the hybridization conditions to the selective polynucleotide, whereby the presence of the selective polynucleotide can be determined.

Probes which are specific for polynucleotides of the present invention can also be prepared using involve transcription-based systems, e.g., incorporating an RNA polymerase promoter into a selective polynucleotide of the present invention, and then transcribing anti-sense RNA using the polynucleotide as a template. See, e.g., U.S. Pat. No. 5,545,522.

Polynucleotide composition

A polynucleotide according to the present invention can comprise, e.g., DNA, RNA, synthetic polynucleotide, peptide polynucleotide, modified nucleotides, dsDNA, ssDNA, ssRNA, dsRNA, and mixtures thereof. A polynucleotide can be single- or double-stranded, triplex, DNA:RNA, duplexes, comprise hairpins, and other secondary structures, etc. Nucleotides comprising a polynucleotide can be joined via various known linkages, e.g., ester, sulfamate, sulfamide, phosphorothioate, phosphoramidate, methylphosphonate, carbamate, etc., depending on the desired purpose, e.g., resistance to nucleases, such as

RNAse H, improved *in vivo* stability, etc. See, e.g., U.S. Pat. No. 5,378,825. Any desired nucleotide or nucleotide analog can be incorporated, e.g., 6-mercaptoguanine, 8-oxo-guanine, etc.

Various modifications can be made to the polynucleotides, such as attaching 5 detectable markers (avidin, biotin, radioactive elements, fluorescent tags and dyes, energy transfer labels, energy-emitting labels, binding partners, etc.) or moieties which improve hybridization, detection, and/or stability. The polynucleotides can also be attached to solid supports, e.g., nitrocellulose, magnetic or paramagnetic microspheres (e.g., as described in U.S. Pat. No. 5,411,863; U.S. Pat. No. 5,543,289; for instance, comprising ferromagnetic, 10 supermagnetic, paramagnetic, superparamagnetic, iron oxide and polysaccharide), nylon, agarose, diazotized cellulose, latex solid microspheres, polyacrylamides, etc., according to a desired method. See, e.g., U.S. Pat. Nos. 5,470,967, 5,476,925, and 5,478,893.

Polynucleotide according to the present invention can be labeled according to any 15 desired method. The polynucleotide can be labeled using radioactive tracers such as ^{32}P , ^{35}S , ^{3}H , or ^{14}C , to mention some commonly used tracers. The radioactive labeling can be carried out according to any method, such as, for example, terminal labeling at the 3' or 5' end using a radiolabeled nucleotide, polynucleotide kinase (with or without dephosphorylation with a phosphatase) or a ligase (depending on the end to be labeled). A non-radioactive labeling can also be used, combining a polynucleotide of the present invention with residues having 20 immunological properties (antigens, haptens), a specific affinity for certain reagents (ligands), properties enabling detectable enzyme reactions to be completed (enzymes or coenzymes, enzyme substrates, or other substances involved in an enzymatic reaction), or characteristic physical properties, such as fluorescence or the emission or absorption of light at a desired wavelength, etc.

25

Nucleic acid detection methods

Another aspect of the present invention relates to methods and processes for detecting tissue selective genes. Detection methods have a variety of applications, including for diagnostic, prognostic, forensic, and research applications. To accomplish gene detection, a 30 polynucleotide in accordance with the present invention can be used as a "probe." The term "probe" or "polynucleotide probe" has its customary meaning in the art, e.g., a polynucleotide

which is effective to identify (e.g., by hybridization), when used in an appropriate process, the presence of a target polynucleotide to which it is designed. Identification can involve simply determining presence or absence, or it can be quantitative, e.g., in assessing amounts of a gene or gene transcript present in a sample. Probes can be useful in a variety of ways, 5 such as for diagnostic purposes, to identify homologs, and to detect, quantitate, or isolate a polynucleotide of the present invention in a test sample.

Assays can be utilized which permit quantification and/or presence/absence detection of a target nucleic acid in a sample. Assays can be performed at the single-cell level, or in a sample comprising many cells, where the assay is "averaging" expression over the entire 10 collection of cells and tissue present in the sample. Any suitable assay format can be used, including, but not limited to, e.g., Southern blot analysis, Northern blot analysis, polymerase chain reaction ("PCR") (e.g., Saiki et al., *Science*, 241:53, 1988; U.S. Pat. Nos. 4,683,195, 4,683,202, and 6,040,166; *PCR Protocols: A Guide to Methods and Applications*, Innis et al., eds., Academic Press, New York, 1990), reverse transcriptase polymerase chain reaction 15 ("RT-PCR"), anchored PCR, rapid amplification of cDNA ends ("RACE") (e.g., Schaefer in *Gene Cloning and Analysis: Current Innovations*, Pages 99-115, 1997), ligase chain reaction ("LCR") (EP 320 308), one-sided PCR (Ohara et al., *Proc. Natl. Acad. Sci.*, 86:5673-5677, 1989), indexing methods (e.g., U.S. Pat. No. 5,508,169), *in situ* hybridization, differential display (e.g., Liang et al., *Nucl. Acid. Res.*, 21:3269-3275, 1993; U.S. Pat. Nos. 5,262,311, 20 5,599,672 and 5,965,409; WO97/18454; Prashar and Weissman, *Proc. Natl. Acad. Sci.*, 93:659-663, and U.S. Pat. Nos. 6,010,850 and 5,712,126; Welsh et al., *Nucleic Acid Res.*, 20:4965-4970, 1992, and U.S. Pat. No. 5,487,985) and other RNA fingerprinting techniques, nucleic acid sequence based amplification ("NASBA") and other transcription based 25 amplification systems (e.g., U.S. Pat. Nos. 5,409,818 and 5,554,527; WO 88/10315), polynucleotide arrays (e.g., U.S. Pat. Nos. 5,143,854, 5,424,186; 5,700,637, 5,874,219, and 6,054,270; PCT WO 92/10092; PCT WO 90/15070), Qbeta Replicase (PCT/US87/00880), Strand Displacement Amplification ("SDA"), Repair Chain Reaction ("RCR"), nuclease protection assays, subtraction-based methods, Rapid-Scan™, etc. Additional useful methods include, but are not limited to, e.g., template-based amplification methods, competitive PCR 30 (e.g., U.S. Pat. No. 5,747,251), redox-based assays (e.g., U.S. Pat. No. 5,871,918), Taqman-based assays (e.g., Holland et al., *Proc. Natl. Acad. Sci.*, 88:7276-7280, 1991; U.S. Pat. Nos.

5,210,015 and 5,994,063), real-time fluorescence-based monitoring (e.g., U.S. Pat. 5,928,907), molecular energy transfer labels (e.g., U.S. Pat. Nos. 5,348,853, 5,532,129, 5,565,322, 6,030,787, and 6,117,635; Tyagi and Kramer, *Nature Biotech.*, 14:303-309, 1996). Any method suitable for single cell analysis of gene or protein expression can be used, including *in situ* hybridization, immunocytochemistry, MACS, FACS, flow cytometry, etc. For single cell assays, expression products can be measured using antibodies, PCR, or other types of nucleic acid amplification (e.g., Brady et al., *Methods Mol. & Cell. Biol.* 2, 17-25, 1990; Eberwine et al., 1992, *Proc. Natl. Acad. Sci.*, 89, 3010-3014, 1992; U.S. Pat. No. 5,723,290). These and other methods can be carried out conventionally, e.g., as described in the mentioned publications.

Many of such methods may require that the polynucleotide is labeled, or comprises a particular nucleotide type useful for detection. The present invention includes such modified polynucleotides that are necessary to carry out such methods. Thus, polynucleotides can be DNA, RNA, DNA:RNA hybrids, PNA, etc., and can comprise any modification or substituent which is effective to achieve detection.

Detection can be desirable for a variety of different purposes, including research, diagnostic, prognostic, and forensic. For diagnostic purposes, it may be desirable to identify the presence or quantity of a polynucleotide sequence in a sample, where the sample is obtained from tissue, cells, body fluids, etc. In a preferred method as described in more detail below, the present invention relates to a method of detecting a polynucleotide comprising, contacting a target polynucleotide in a test sample with a polynucleotide probe under conditions effective to achieve hybridization between the target and probe; and detecting hybridization.

Any test sample in which it is desired to identify a polynucleotide or polypeptide thereof can be used, including, e.g., blood, urine, saliva, stool (for extracting nucleic acid, see, e.g., U.S. Pat. No. 6,177,251), swabs comprising tissue, biopsied tissue, tissue sections, cultured cells, etc.

Detection can be accomplished in combination with polynucleotide probes for other genes, e.g., genes which are expressed in other disease states, tissues, cells, such as brain, heart, kidney, spleen, thymus, liver, stomach, small intestine, colon, muscle, lung, testis, placenta, pituitary, thyroid, skin, adrenal gland, pancreas, salivary gland, uterus, ovary,

prostate gland, peripheral blood cells (T-cells, lymphocytes, etc.), embryo, breast, fat, adult and embryonic stem cells, etc.

Polynucleotides can be used in wide range of methods and compositions, including for detecting, diagnosing, staging, grading, assessing, prognosticating, etc. diseases and disorders associated with tissue selective genes, for monitoring or assessing therapeutic and/or preventative measures, in ordered arrays, etc. Any method of detecting genes and polynucleotides can be used; certainly, the present invention is not to be limited how such methods are implemented.

Along these lines, the present invention relates to methods of detecting

polynucleotides of the present invention in a sample comprising nucleic acid. Such methods can comprise one or more the following steps in any effective order, e.g., contacting said sample with a polynucleotide probe under conditions effective for said probe to hybridize specifically to nucleic acid in said sample, and detecting the presence or absence of probe hybridized to nucleic acid in said sample, wherein said probe is a polynucleotide which is described herein, a polynucleotide having, e.g., about 70%, 80%, 85%, 90%, 95%, 99%, or more sequence identity thereto, effective or specific fragments thereof, or complements thereto. The detection method can be applied to any sample, e.g., cultured primary, secondary, or established cell lines, tissue biopsy, blood, urine, stool, cerebral spinal fluid, and other bodily fluids, for any purpose.

Contacting the sample with probe can be carried out by any effective means in any effective environment. It can be accomplished in a solid, liquid, frozen, gaseous, amorphous, solidified, coagulated, colloid, etc., mixtures thereof, matrix. For instance, a probe in an aqueous medium can be contacted with a sample which is also in an aqueous medium, or which is affixed to a solid matrix, or vice-versa.

Generally, as used throughout the specification, the term "effective conditions" means, e.g., the particular milieu in which the desired effect is achieved. Such a milieu, includes, e.g., appropriate buffers, oxidizing agents, reducing agents, pH, co-factors, temperature, ion concentrations, suitable age and/or stage of cell (such as, in particular part of the cell cycle, or at a particular stage where particular genes are being expressed) where cells are being used, culture conditions (including substrate, oxygen, carbon dioxide, etc.). When hybridization is the chosen means of achieving detection, the probe and sample can be

combined such that the resulting conditions are functional for said probe to hybridize specifically to nucleic acid in said sample.

The phrase "hybridize specifically" indicates that the hybridization between single-stranded polynucleotides is based on nucleotide sequence complementarity. The effective 5 conditions are selected such that the probe hybridizes to a preselected and/or definite target nucleic acid in the sample. For instance, if detection of a polynucleotide set forth herein is desired, a probe can be selected which can hybridize to such target gene under high stringent conditions, without significant hybridization to other genes in the sample. To detect homologs of a polynucleotide set forth in herein, the effective hybridization conditions can be 10 less stringent, and/or the probe can comprise codon degeneracy, such that a homolog is detected in the sample.

As already mentioned, the methods can be carried out by any effective process, e.g., by Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, *in situ* hybridization, etc., as indicated above. When PCR based techniques are 15 used, two or more probes are generally used. One probe can be specific for a defined sequence which is characteristic of a selective polynucleotide, but the other probe can be specific for the selective polynucleotide, or specific for a more general sequence, e.g., a sequence such as polyA which is characteristic of mRNA, a sequence which is specific for a promoter, ribosome binding site, or other transcriptional features, a consensus sequence (e.g., 20 representing a functional domain). For the former aspects, 5' and 3' probes (e.g., polyA, Kozak, etc.) are preferred which are capable of specifically hybridizing to the ends of transcripts. When PCR is utilized, the probes can also be referred to as "primers" in that they can prime a DNA polymerase reaction.

In addition to testing for the presence or absence of polynucleotides, the present 25 invention also relates to determining the amounts at which polynucleotides of the present invention are expressed in sample and determining the differential expression of such polynucleotides in samples.. Such methods can involve substantially the same steps as described above for presence/absence detection, e.g., contacting with probe, hybridizing, and detecting hybridized probe, but using more quantitative methods and/or comparisons to 30 standards.

The amount of hybridization between the probe and target can be determined by any suitable methods, e.g., PCR, RT-PCR, RACE PCR, Northern blot, polynucleotide microarrays, Rapid-Scan, etc., and includes both quantitative and qualitative measurements.

For further details, see the hybridization methods described above and below. Determining

- 5 by such hybridization whether the target is differentially expressed (e.g., up-regulated or down-regulated) in the sample can also be accomplished by any effective means. For instance, the target's expression pattern in the sample can be compared to its pattern in a known standard, such as in a normal tissue, or it can be compared to another gene in the same sample. When a second sample is utilized for the comparison, it can be a sample of normal
10 tissue that is known not to contain diseased cells. The comparison can be performed on samples which contain the same amount of RNA (such as polyadenylated RNA or total RNA), or, on RNA extracted from the same amounts of starting tissue. Such a second sample can also be referred to as a control or standard. Hybridization can also be compared to a second target in the same tissue sample. Experiments can be performed that determine a
15 ratio between the target nucleic acid and a second nucleic acid (a standard or control), e.g., in a normal tissue. When the ratio between the target and control are substantially the same in a normal and sample, the sample is determined or diagnosed not to contain cells. However, if the ratio is different between the normal and sample tissues, the sample is determined to contain, e.g., kidney, pancreas, or immune cells. The approaches can be combined, and one
20 or more second samples, or second targets can be used. Any second target nucleic acid can be used as a comparison, including "housekeeping" genes, such as beta-actin, alcohol dehydrogenase, or any other gene whose expression does not vary depending upon the disease status of the cell.

25 Methods of identifying polymorphisms, mutations, etc.

Polynucleotides of the present invention can also be utilized to identify mutant alleles, SNPs, gene rearrangements and modifications, and other polymorphisms of the wild-type gene. Mutant alleles, polymorphisms, SNPs, etc., can be identified and isolated from subjects with diseases that are known, or suspected to have, a genetic component.

- 30 Identification of such genes can be carried out routinely (see, above for more guidance), e.g., using PCR, hybridization techniques, direct sequencing, mismatch reactions (see, e.g.,

above), RFLP analysis, SSCP (e.g., Orita et al., *Proc. Natl. Acad. Sci.*, 86:2766, 1992), etc., where a polynucleotide having a sequence selected from the polynucleotides of the present invention is used as a probe. The selected mutant alleles, SNPs, polymorphisms, etc., can be used diagnostically to determine whether a subject has, or is susceptible to a disorder 5 associated with tissue selective genes disclosed herein, as well as to design therapies and predict the outcome of the disorder. Methods involve, e.g., diagnosing a disorder or determining susceptibility to a disorder, comprising, detecting the presence of a mutation in a gene represented by a polynucleotide selected from the sequences disclosed herein. The detecting can be carried out by any effective method, e.g., obtaining cells from a subject, 10 determining the gene sequence or structure of a target gene (using, e.g., mRNA, cDNA, genomic DNA, etc), comparing the sequence or structure of the target gene to the structure of the normal gene, whereby a difference in sequence or structure indicates a mutation in the gene in the subject. Polynucleotides can also be used to test for mutations, SNPs, polymorphisms, etc., e.g., using mismatch DNA repair technology as described in U.S. Pat. 15 No. 5,683,877; U.S. Pat. No. 5,656,430; Wu et al., *Proc. Natl. Acad. Sci.*, 89:8779-8783, 1992.

The present invention also relates to methods of detecting polymorphisms in tissue selective genes, comprising, e.g., comparing the structure of: genomic DNA comprising all or part of a tissue selective gene, mRNA comprising all or part of a tissue selective gene, cDNA 20 comprising all or part of a tissue selective gene, or a polypeptide comprising all or part of a tissue selective gene, with the structure the polynucleotides set forth herein. The methods can be carried out on a sample from any source, e.g., cells, tissues, body fluids, blood, urine, stool, hair, egg, sperm, cerebral spinal fluid, biopsy samples, serum, etc.

These methods can be implemented in many different ways. For example, 25 "comparing the structure" steps include, but are not limited to, comparing restriction maps, nucleotide sequences, amino acid sequences, RFLPs, Dnase sites, DNA methylation fingerprints (e.g., U.S. Pat. No. 6,214,556), protein cleavage sites, molecular weights, electrophoretic mobilities, charges, ion mobility, etc., between standard and a test genes. The term "structure" can refer to any physical characteristics or configurations which can be used 30 to distinguish between nucleic acids and polypeptides. The methods and instruments used to accomplish the comparing step depends upon the physical characteristics which are to be

compared. Thus, various techniques are contemplated, including, e.g., sequencing machines (both amino acid and polynucleotide), electrophoresis, mass spectrometer (U.S. Pat. Nos. 6,093,541, 6,002,127), liquid chromatography, HPLC, etc.

To carry out such methods, "all or part" of the gene or polypeptide can be compared.

- 5 For example, if nucleotide sequencing is utilized, the entire gene can be sequenced, including promoter, introns, and exons, or only parts of it can be sequenced and compared, e.g., exon 1, exon 2, etc.

Mutagenesis

- 10 Mutated polynucleotide sequences of the present invention are useful for various purposes, e.g., to create mutations of the polypeptides they encode, to identify functional regions of genomic DNA, to produce probes for screening libraries, etc. Mutagenesis can be carried out routinely according to any effective method, e.g., oligonucleotide-directed (Smith, M., *Ann. Rev. Genet.* 19:423-463, 1985), degenerate oligonucleotide-directed (Hill et al., 15 *Method Enzymology*, 155:558-568, 1987), region-specific (Myers et al., *Science*, 229:242-246, 1985; Derbyshire et al., *Gene*, 46:145, 1986; Ner et al., *DNA*, 7:127, 1988), linker-scanning (McKnight and Kingsbury, *Science*, 217:316-324, 1982), directed using PCR, recursive ensemble mutagenesis (Arkin and Yourvan, *Proc. Natl. Acad. Sci.*, 89:7811-7815, 1992), random mutagenesis (e.g., U.S. Pat. Nos. 5,096,815; 5,198,346; and 5,223,409), site-directed mutagenesis (e.g., Walder et al., *Gene*, 42:133, 1986; Bauer et al., *Gene*, 37:73, 1985; Craik, *Bio Techniques*, January 1985, 12-19; Smith et al., *Genetic Engineering: Principles and Methods*, Plenum Press, 1981), phage display (e.g., Lowman et al., *Biochem.* 30:10832-10837, 1991; Ladner et al., U.S. Pat. No. 5,223,409; Huse, WIPO Publication WO 92/06204), etc. Desired sequences can also be produced by the assembly of target sequences 20 using mutually priming oligonucleotides (Uhlmann, *Gene*, 71:29-40, 1988). For directed mutagenesis methods, analysis of the three-dimensional structure of the polypeptide can be used to guide and facilitate making mutants which effect polypeptide activity. Sites of substrate-enzyme interaction or other biological activities can also be determined by analysis 25 of crystal structure as determined by such techniques as nuclear magnetic resonance, crystallography or photoaffinity labeling. See, for example, de Vos et al., *Science* 255:306-312, 1992; Smith et al., *J. Mol. Biol.* 224:899-904, 1992; Wlodaver et al., *FEBS Lett.* 30

309:59-64, 1992.

In addition, libraries of genes and fragments thereof can be used for screening and selection of genes variants. For instance, a library of coding sequences can be generated by treating a double-stranded DNA with a nuclease under conditions where the nicking occurs, 5 e.g., only once per molecule, denaturing the double-stranded DNA, renaturing it to form double-stranded DNA that can include sense/antisense pairs from different nicked products, removing single-stranded portions from reformed duplexes by treatment with S1 nuclease, and ligating the resulting DNAs into an expression vector. By this method, expression libraries can be made comprising "mutagenized" tissue selective genes. The entire coding 10 sequence or parts thereof can be used.

Polynucleotide expression, polypeptides produced thereby, and specific-binding partners thereto.

A polynucleotide according to the present invention can be expressed in a variety of 15 different systems, in vitro and in vivo, according to the desired purpose. For example, a polynucleotide can be inserted into an expression vector, introduced into a desired host, and cultured under conditions effective to achieve expression of a polypeptide coded for by the polynucleotide, to search for specific binding partners. Effective conditions include any culture conditions which are suitable for achieving production of the polypeptide by the host 20 cell, including effective temperatures, pH, medium, additives to the media in which the host cell is cultured (e.g., additives which amplify or induce expression such as butyrate, or methotrexate if the coding polynucleotide is adjacent to a dhfr gene), cycloheximide, cell densities, culture dishes, etc. A polynucleotide can be introduced into the cell by any effective method including, e.g., naked DNA, calcium phosphate precipitation, 25 electroporation, injection, DEAE-Dextran mediated transfection, fusion with liposomes, association with agents which enhance its uptake into cells, viral transfection. A cell into which a polynucleotide of the present invention has been introduced is a transformed host cell. The polynucleotide can be extrachromosomal or integrated into a chromosome(s) of the host cell. It can be stable or transient. An expression vector is selected for its compatibility 30 with the host cell. Host cells include, mammalian cells, e.g., COS, CV1, BHK, CHO, HeLa, LTK, NIH 3T3, insect cells, such as Sf9 (*S. frugipeda*) and *Drosophila*, bacteria, such as *E.*

coli, Streptococcus, bacillus, yeast, such as Sacharomyces, S. cerevisiae, fungal cells, plant cells, embryonic or adult stem cells (e.g., mammalian, such as mouse or human),

immune system cell lines, HH (ATCC CRL 2105), MOLT-4 (ATCC CRL 1582), MJ (ATCC CRL-8294), SK7 (ATCC HB-8584), SK8 (ATCC HB-8585), HM1 (HB-8586), H9 5 (ATCC HTB-176), HuT 78 (ATCC TIB-161), HuT 102 (ATCC TIB-162), Jurkat,

B-cell lines, B-cell precursor lines, NALM-36, B-cell and other lymphocyte lines immortalized with Epstein-Barr virus (transformed B lymphoblastoid), stromal cell lines, myelomas, HBM-Noda, WEHI231,

10 reticuloendothelial cells, endothelial cells, white blood cells, macrophages, antigen-presenting cells, lymphocytes, GDM-1 (ATCC CRL-2627), THP-1 (ATCC TIB-202), HL-60 (ATCC CCL-240), and derivatives thereof, including primary and established cell lines thereof,

15 kidney cell lines, 293, G-402 (ATCC CRL-1440), ACHN (ATCC CRL-1611), Vero (ATCC CCL-81), 786-O (ATCC CRL-1932), 769-P (ATCC CRL-1933), CCD 1103 KIDTr (ATCC CRL-2304), CCD 1105 KIDTr (ATCC CRL-2305), Hs 835.T (ATCC CRL-7569), Hs 926.T (ATCC CRL-7678), Caki-1 (ATCC HTB-46), Caki-2 (ATCC HTB-47), SW 839 (ATCC HTB-49), LLC-MK2 (ATCC CCL-7), BHK-21 (ATCC CCL-10), MDCK, CV-1, (ATCC CRL-1573), KNRK (ATCC CRL-1569), NRK-49F (ATCC CRL-1570), A-704 (ATCC HTB-45), etc., established and primary kidney cells,

20 pancreas cell lines, , insulinoma cell lines, INS-H1, MIN6N8, RIN 1046-38, RIN-5AH, RIN-A12, RINm5F, capan-1, capan-2, MIA PaCa-2 (ATCC CRL-1420), PANC-1 (ATCC CRL-1469), AsPC-1 (ATCC CRL-1682), SU-86.86 (ATCC CRL-1837), CFPAC-1 (ATCC CRL-1918), HPAF-II (ATCC CRL-1937), TGP61 (ATCC CRL-2135) and other TGP lines, SW 1990 (ATCC CRL-2172), Mpanc-96 (ATCC CRL-2380), MSI VEGF

25 (ATCC CRL-2460), Beta-TC-6 (ATCC CRL-11506), LTPA (ATCC CRL-2389), 266-6 (ATCC CRL-2151), MSI (ATCC CRL-2779), SVR (ATCC CRL-2280), NIT-2 (ATCC CRL-2364), alphaTC1 Clone 9 (ATCC CRL-2350), ATCC CRL-1492, BxPC-3 (ATCC CRL-1687), HPAC (ATCC CRL-2119), U.S. Pat. Nos. 6,110743, 5,928,942, 5,888,816, 5,888,705, and 5,723,333, etc., established and primary pancreas cells (e.g., according to

30 Hellerstrom et al., *Diabetes*, 28:769-76, 1979),

- retinal cell lines, RF/6A (CRL 1780), ARPE-19 (CRL-2302), ARPE-19/HPV-16 (CRL-2502), Y79 (HTB-18), WERI-Rb-1 (HTB-169), RPE-J (CRL-2240), SO-Rb50 (retinoblastoma cell line), RBL, HER-Xho1-CC2, WERI-Rb24 (Sery et al., *J. Pediatr. Ophthalmol. Strabismus*, 4:212-217, 1990), WERI-Rb27 (Sery et al., *J. Pediatr. Ophthalmol. Strabismus*, 4:212-217, 1990), HXO-Rb44, fetal retina cells, retinoblastoma cells, choroidal endothelial cells (e.g., Chor 55), etc., established and primary retinal cells (For other cell lines and methods thereof, see, also, Griege et al, *Differentiation*, 45:250-7, 1990; Bernstein et al., *Invest. Ophthalmol. Vis. Sci.*, 35:3931-3937, 1994; Howes et al., *Invest. Ophthalmol. Vis. Sci.*, 35:342-351, 1994).
- 10 Expression control sequences are similarly selected for host compatibility and a desired purpose, e.g., high copy number, high amounts, induction, amplification, controlled expression. Other sequences which can be employed include enhancers such as from SV40, CMV, RSV, inducible promoters, cell-type specific elements, or sequences which allow selective or specific cell expression. Promoters that can be used to drive its expression, 15 include, e.g., the endogenous promoter, MMTV, SV40, trp, lac, tac, or T7 promoters for bacterial hosts; or alpha factor, alcohol oxidase, or PGH promoters for yeast. RNA promoters can be used to produced RNA transcripts, such as T7 or SP6. See, e.g., Melton et al., *Polynucleotide Res.*, 12(18):7035-7056, 1984; Dunn and Studier. *J. Mol. Bio.*, 166:477-435, 1984; U.S. Pat. No. 5,891,636; Studier et al., *Gene Expression Technology, Methods in Enzymology*, 85:60-89, 1987. In addition, as discussed above, translational signals (including 20 in-frame insertions) can be included.

When a polynucleotide is expressed as a heterologous gene in a transfected cell line, the gene is introduced into a cell as described above, under effective conditions in which the gene is expressed. The term "heterologous" means that the gene has been introduced into the 25 cell line by the "hand-of-man." Introduction of a gene into a cell line is discussed above. The transfected (or transformed) cell expressing the gene can be lysed or the cell line can be used intact.

For expression and other purposes, a polynucleotide can contain codons found in a naturally-occurring gene, transcript, or cDNA, for example, e.g., as set forth in herein or it 30 can contain degenerate codons coding for the same amino acid sequences. For instance,

it may be desirable to change the codons in the sequence to optimize the sequence for expression in a desired host. See, e.g., U.S. Pat. Nos. 5,567,600 and 5,567,862.

A polypeptide according to the present invention can be recovered from natural sources, transformed host cells (culture medium or cells) according to the usual methods, 5 including, detergent extraction (e.g., non-ionic detergent, Triton X-100, CHAPS, octylglucoside, Igepal CA-630), ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxyapatite chromatography, lectin chromatography, gel electrophoresis. Protein refolding steps can be used, as necessary, in completing the 10 configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for purification steps. Another approach is express the polypeptide recombinantly with an affinity tag (Flag epitope, HA epitope, myc epitope, 6xHis, maltose binding protein, chitinase, etc) and then purify by anti-tag antibody-conjugated affinity chromatography.

15 The present invention also relates to specific-binding partners. These include antibodies which are specific for polypeptides encoded by polynucleotides of the present invention, as well as other binding-partners which interact with polynucleotides and polypeptides of the present invention. Protein-protein interactions between polypeptides and binding partners can be identified using any suitable methods, e.g., protein binding assays 20 (e.g., filtration assays, chromatography, etc.), yeast two-hybrid system (Fields and Song, *Nature*, 340: 245-247, 1989), protein arrays, gel-shift assays, FRET (fluorescence resonance energy transfer) assays, etc. Nucleic acid interactions (e.g., protein-DNA or protein-RNA) can be assessed using gel-shift assays, e.g., as carried out in U.S. Pat. No. 6,333,407 and 5,789,538.

25 Antibodies, e.g., polyclonal, monoclonal, recombinant, chimeric, humanized, single-chain, Fab, and fragments thereof, can be prepared according to any desired method. Antibodies, and immune responses, can also be generated by administering naked DNA See, e.g., U.S. Pat. Nos. 5,703,055; 5,589,466; 5,580,859. Antibodies can be used from any source, including, goat, rabbit, mouse, chicken (e.g., IgY; see, Duan, WO/029444 for methods 30 of making antibodies in avian hosts, and harvesting the antibodies from the eggs). An antibody specific for a polypeptide means that the antibody recognizes a defined sequence of

amino acids within or including the polypeptide. Other specific binding partners include, e.g., aptamers and PNA. Antibodies can be prepared against specific epitopes or domains.

Antibodies can also be humanized, e.g., where they are to be used therapeutically.

Methods for obtaining human antibodies, e.g., from transgenic mice are described, e.g., in

5 Green et al., Nature Genet. 7:13 (1994); Lonberg et al., Nature 368:856 (1994); and Taylor et al., Int. Immunol. 6:579 (1994). Antibody fragments of the present invention can be prepared by any suitable method, Fab and Fc fragments. single-chain antibodies can also be used. Another form of an antibody fragment is a peptide coding for a single complementarity-determining region (CDR). CDR peptides ("minimal recognition units") can be obtained by
10 constructing genes encoding the CDR of an antibody of interest.

The term "antibody" as used herein includes intact molecules as well as fragments thereof, such as Fab, F(ab')2, and Fv which are capable of binding to an epitopic determinant present in Bin1 polypeptide. Such antibody fragments retain some ability to selectively bind with its antigen or receptor. The term "epitope" refers to an antigenic determinant on an
15 antigen to which the paratope of an antibody binds. Epitopic determinants usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Antibodies can be prepared against specific epitopes or polypeptide domains.

20 Antibodies which bind to polypeptides of the present invention can be prepared using an intact polypeptide or fragments containing small peptides of interest as the immunizing antigen. For example, it may be desirable to produce antibodies that specifically bind to the N- or C-terminal domains of the tissue selective polypeptides of the present invention. The polypeptide or peptide used to immunize an animal which is derived from translated cDNA
25 or chemically synthesized which can be conjugated to a carrier protein, if desired. Such commonly used carriers which are chemically coupled to the immunizing peptide include keyhole limpet hemocyanin (KLH), thyroglobulin, bovine serum albumin (BSA), and tetanus toxoid.

30 Methods of detecting polypeptides

Polypeptides coded for by genes of the present invention can be detected, visualized, determined, quantitated, etc. according to any effective method. Useful methods include, e.g., but are not limited to, immunoassays, RIA (radioimmunassay), ELISA, (enzyme-linked-immunosorbent assay), immunofluorescence, flow cytometry, histology, electron microscopy, 5 light microscopy, *in situ* assays, immunoprecipitation, Western blot, etc.

Immunoassays may be carried in liquid or on biological support. For instance, a sample (e.g., blood, serum, stool, urine, cells, tissue, cerebral spinal fluid, body fluids, etc.) can be brought in contact with and immobilized onto a solid phase support or carrier such as nitrocellulose, or other solid support that is capable of immobilizing cells, cell particles or 10 soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled specific antibody. The solid phase support can then be washed with a buffer a second time to remove unbound antibody. The amount of bound label on solid support may then be detected by conventional means.

A "solid phase support or carrier" includes any support capable of binding an antigen, 15 antibody, or other specific binding partner. Supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, and magnetite. A support material can have any structural or physical configuration. Thus, the support configuration may be spherical, as in a bead, or cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the 20 surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads.

One of the many ways in which gene peptide-specific antibody can be detectably labeled is by linking it to an enzyme and using it in an enzyme immunoassay (EIA). See, e.g., Voller, A., "The Enzyme Linked Immunosorbent Assay (ELISA)," 1978, Diagnostic 25 Horizons 2, 1-7, Microbiological Associates Quarterly Publication, Walkersville, Md.); Voller, A. et al., 1978, J. Clin. Pathol. 31, 507-520; Butler, J. E., 1981, Meth. Enzymol. 73, 482-523; Maggio, E. (ed.), 1980, Enzyme Immunoassay, CRC Press, Boca Raton, Fla.. The enzyme which is bound to the antibody will react with an appropriate substrate, preferably a chromogenic substrate, in such a manner as to produce a chemical moiety that can be 30 detected, for example, by spectrophotometric, fluorimetric or by visual means. Enzymes that can be used to detectably label the antibody include, but are not limited to, malate

dehydrogenase, staphylococcal nuclease, delta-5-steroid isomerase, yeast alcohol dehydrogenase, .alpha.-glycerophosphate dehydrogenase, triose phosphate isomerase, horseradish peroxidase, alkaline phosphatase, asparaginase, glucose oxidase, .beta.-galactosidase, ribonuclease, urease, catalase, glucose-6-phosphate dehydrogenase, 5 glucoamylase and acetylcholinesterase. The detection can be accomplished by colorimetric methods that employ a chromogenic substrate for the enzyme. Detection may also be accomplished by visual comparison of the extent of enzymatic reaction of a substrate in comparison with similarly prepared standards.

Detection may also be accomplished using any of a variety of other immunoassays.

10 For example, by radioactively labeling the antibodies or antibody fragments, it is possible to detect peptides through the use of a radioimmunoassay (RIA). See, e.g., Weintraub, B., Principles of Radioimmunoassays, Seventh Training Course on Radioligand Assay Techniques, The Endocrine Society, March, 1986. The radioactive isotope can be detected by such means as the use of a gamma counter or a scintillation counter or by autoradiography.

15 It is also possible to label the antibody with a fluorescent compound. When the fluorescently labeled antibody is exposed to light of the proper wave length, its presence can then be detected due to fluorescence. Among the most commonly used fluorescent labeling compounds are fluorescein isothiocyanate, rhodamine, phycoerythrin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine. The antibody can also be detectably 20 labeled using fluorescence emitting metals such as those in the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

The antibody also can be detectably labeled by coupling it to a chemiluminescent compound. The presence of the chemiluminescent-tagged antibody is then determined by 25 detecting the presence of luminescence that arises during the course of a chemical reaction. Examples of useful chemiluminescent labeling compounds are luminol, isoluminol, theromatic acridinium ester, imidazole, acridinium salt and oxalate ester.

Likewise, a bioluminescent compound may be used to label the antibody of the present invention. Bioluminescence is a type of chemiluminescence found in biological 30 systems in which a catalytic protein increases the efficiency of the chemiluminescent reaction. The presence of a bioluminescent protein is determined by detecting the presence of

luminescence. Important bioluminescent compounds for purposes of labeling are luciferin, luciferase and aequorin.

Diagnostic

5 The present invention also relates to methods and compositions for diagnosing a disorder, or determining susceptibility to a disorder, using polynucleotides, polypeptides, and specific-binding partners of the present invention to detect, assess, determine, etc., a tissue selective gene. In such methods, the gene can serve as a marker for the disorder, e.g., where the gene, when mutant, is a direct cause of the disorder; where the gene is affected by another
10 gene(s) which is directly responsible for the disorder, e.g., when the gene is part of the same signaling pathway as the directly responsible gene; and, where the gene is chromosomally linked to the gene(s) directly responsible for the disorder, and segregates with it. Many other situations are possible. To detect, assess, determine, etc., a probe specific for the gene can be employed as described above and below. Any method of detecting and/or assessing the gene
15 can be used, including detecting expression of the gene using polynucleotides, antibodies, or other specific-binding partners.

The phrase "diagnosing" indicates that it is determined whether the sample has the disorder. A "disorder" means, e.g., any abnormal condition as in a disease or malady. "Determining a subject's susceptibility to a disease or disorder" indicates that the subject is
20 assessed for whether s/he is predisposed to get such a disease or disorder, where the predisposition is indicated by abnormal expression of the gene (e.g., gene mutation, gene expression pattern is not normal, etc.). Predisposition or susceptibility to a disease may result when a such disease is influenced by epigenetic, environmental, etc., factors. Diagnosing includes prenatal screening where samples from the fetus or embryo (e.g., via amniocentesis
25 or CV sampling) are analyzed for the expression of the gene.

By the phrase "assessing expression of a gene or polynucleotide," it is meant that the functional status of the gene is evaluated. This includes, but is not limited to, measuring expression levels of said gene, determining the genomic structure of said gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of
30 polypeptide coded for by said gene. Thus, the term "assessing expression" includes evaluating the all aspects of the transcriptional and translational machinery of the gene. For

instance, if a promoter defect causes, or is suspected of causing, the disorder, then a sample can be evaluated (i.e., "assessed") by looking (e.g., sequencing or restriction mapping) at the promoter sequence in the gene, by detecting transcription products (e.g., RNA), by detecting translation product (e.g., polypeptide). Any measure of whether the gene is functional can be 5 used, including, polypeptide, polynucleotide, and functional assays for the gene's biological activity.

In making the assessment, it can be useful to compare the results to a normal gene, e.g., a gene which is not associated with the disorder. The nature of the comparison can be determined routinely, depending upon how the assessing is accomplished. If, for example, 10 the mRNA levels of a sample is detected, then the mRNA levels of a normal can serve as a comparison, or a gene which is known not to be affected by the disorder. Methods of detecting mRNA are well known, and discussed above, e.g., but not limited to, Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, etc. Similarly, if polypeptide production is used to evaluate the gene, then the polypeptide in a 15 normal tissue sample can be used as a comparison, or, polypeptide from a different gene whose expression is known not to be affected by the disorder. These are only examples of how such a method could be carried out.

The genes and polypeptides of the present invention can be used to identify, detect, stage, determine the presence of, prognosticate, treat, study, etc., diseases and conditions as 20 mentioned above. The present invention relates to methods of identifying a genetic basis for a disease or disease-susceptibility, comprising, e.g., determining the association of a disease or disease-susceptibility with a gene of the present invention. An association between a disease or disease-susceptibility and nucleotide sequence includes, e.g., establishing (or finding) a correlation (or relationship) between a DNA marker (e.g., gene, VNTR, 25 polymorphism, EST, etc.) and a particular disease state. Once a relationship is identified, the DNA marker can be utilized in diagnostic tests and as a drug target. Any region of the gene can be used as a source of the DNA marker, exons, introns, intergenic regions, etc.

Human linkage maps can be constructed to establish a relationship between a gene and a disease or condition. Typically, polymorphic molecular markers (e.g., STRP's, SNP's, 30 RFLP's, VNTR's) are identified within the region, linkage and map distance between the markers is then established, and then linkage is established between phenotype and the

various individual molecular markers. Maps can be produced for an individual family, selected populations, patient populations, etc. In general, these methods involve identifying a marker associated with the disease (e.g., identifying a polymorphism in a family which is linked to the disease) and then analyzing the surrounding DNA to identify the gene

- 5 responsible for the phenotype. See, e.g., Kruglyak et al., *Am. J. Hum. Genet.*, 58, 1347-1363, 1996; Matise et al., *Nat. Genet.*, 6(4):384-90, 1994.

Assessing the effects of therapeutic and preventative interventions (e.g., administration of a drug, chemotherapy, radiation, etc.) on disorders is a major effort in drug discovery, clinical medicine, and pharmacogenomics. The evaluation of therapeutic and

- 10 preventative measures, whether experimental or already in clinical use, has broad applicability, e.g., in clinical trials, for monitoring the status of a patient, for analyzing and assessing animal models, and in any scenario involving disease treatment and prevention.

Analyzing the expression profiles of polynucleotides of the present invention can be utilized as a parameter by which interventions are judged and measured. Treatment of a disorder can

- 15 change the expression profile in some manner which is prognostic or indicative of the drug's effect on it. Changes in the profile can indicate, e.g., drug toxicity, return to a normal level, etc. Accordingly, the present invention also relates to methods of monitoring or assessing a therapeutic or preventative measure (e.g., chemotherapy, radiation, anti-neoplastic drugs, antibodies, etc.) in a subject having a disorder, or, susceptible to such a disorder, comprising,

- 20 e.g., detecting the expression levels of one or more tissue selective genes. A subject can be a cell-based assay system, non-human animal model, human patient, etc. Detecting can be accomplished as described for the methods above and below. By "therapeutic or preventative intervention," it is meant, e.g., a drug administered to a patient, surgery, radiation, chemotherapy, and other measures taken to prevent, treat, or diagnose a disorder.

- 25 The present invention also relates to methods of using binding partners, such as antibodies, to deliver active agents to the tissue (e.g., kidney or pancreas or an immune cells) for a variety of different purposes, including, e.g., for diagnostic, therapeutic, and research purposes. Methods can involve delivering or administering an active agent to the tissue, comprising, e.g., administering to a subject in need thereof, an effective amount of an active
30 agent coupled to a binding partner specific for a tissue selective polypeptide, wherein said binding partner is effective to deliver said active agent specifically to the target tissue.

Any type of active agent can be used in combination with it, including, therapeutic, cytotoxic, cytostatic, chemotherapeutic, anti-neoplastic, anti-proliferative, anti-biotic, etc., agents. A chemotherapeutic agent can be, e.g., DNA-interactive agent, alkylating agent, antimetabolite, tubulin-interactive agent, hormonal agent, hydroxyurea, Cisplatin,

- 5 Cyclophosphamide, Altretamine, Bleomycin, Dactinomycin, Doxorubicin, Etoposide, Teniposide, paclitaxel, cytoxin, 2-methoxy-carbonyl-amino-benzimidazole, Plicamycin, Methotrexate, Fluorouracil, Fluorodeoxyuridine, CB3717, Azacitidine, Floxuridine, Mercaptopurine, 6-Thioguanine, Pentostatin, Cytarabine, Fludarabine, etc. Agents can also be contrast agents useful in imaging technology, e.g., X-ray, CT, CAT, MRI, ultrasound,
- 10 PET, SPECT, and scintographic.

An active agent can be associated in any manner with a binding partner which is effective to achieve its delivery specifically to the target. Specific delivery or targeting indicates that the agent is provided to the tissue, without being substantially provided to other tissues. This is useful especially where an agent is toxic, and specific targeting to the tissue enables the majority of the toxicity to be aimed at the tissue, with as small as possible effect on other tissues in the body. The association of the active agent and the binding partner ("coupling") can be direct, e.g., through chemical bonds between the binding partner and the agent, or, via a linking agent, or the association can be less direct, e.g., where the active agent is in a liposome, or other carrier, and the binding partner is associated with the liposome surface. In such case, the binding partner can be oriented in such a way that it is able to bind to tissue selective polypeptide, e.g., exposed on the cell surface. Methods for delivery of DNA via a cell-surface receptor is described, e.g., in U.S. Pat. No. 6,339,139.

Identifying agent methods

- 25 The present invention also relates to methods of identifying agents, and the agents themselves, which modulate tissue selective genes. These agents can be used to modulate the biological activity of the polypeptide encoded for the gene, or the gene, itself. Agents which regulate the gene or its product are useful in variety of different environments, including as medicinal agents to treat or prevent disorders associated with genes and as research reagents
- 30 to modify the function of tissues and cell.

Methods of identifying agents generally comprise steps in which an agent is placed in contact with the gene, its transcription product, its translation product, or other target, and then a determination is performed to assess whether the agent "modulates" the target. The specific method utilized will depend upon a number of factors, including, e.g., the target (i.e., 5 is it the gene or polypeptide encoded by it), the environment (e.g., *in vitro* or *in vivo*), the composition of the agent, etc.

For modulating the expression of tissue selective genes, a method can comprise, in any effective order, one or more of the following steps, e.g., contacting a gene (e.g., in a cell population) with a test agent under conditions effective for said test agent to modulate the 10 expression of tissue selective genes, and determining whether said test agent modulates said genes. An agent can modulate expression of a tissue selective gene at any level, including transcription (e.g., by modulating the promoter), translation, and/or perdurance of the nucleic acid (e.g., degradation, stability, etc.) in the cell.

For modulating the biological activity of polypeptides, a method can comprise, in any 15 effective order, one or more of the following steps, e.g., contacting a polypeptide (e.g., in a cell, lysate, or isolated) with a test agent under conditions effective for said test agent to modulate the biological activity of said polypeptide, and determining whether said test agent modulates said biological activity.

Contacting a gene or polypeptide with the test agent can be accomplished by any 20 suitable method and/or means that places the agent in a position to functionally control expression or biological activity. Functional control indicates that the agent can exert its physiological effect through whatever mechanism it works. The choice of the method and/or means can depend upon the nature of the agent and the condition and type of environment in which the gene or polypeptide is presented, e.g., lysate, isolated, or in a cell population (such 25 as, *in vivo*; *in vitro*, organ explants, etc.). For instance, if the cell population is an *in vitro* cell culture, the agent can be contacted with the cells by adding it directly into the culture medium. If the agent cannot dissolve readily in an aqueous medium, it can be incorporated into liposomes, or another lipophilic carrier, and then administered to the cell culture. Contact can also be facilitated by incorporation of agent with carriers and delivery molecules 30 and complexes, by injection, by infusion, etc.

Agents can be directed to, or targeted to, any part of the polypeptide which is

effective for modulating it. For example, agents, such as antibodies and small molecules, can be targeted to cell-surface, exposed, extracellular, ligand binding, functional, etc., domains of the polypeptide. Agents can also be directed to intracellular regions and domains, e.g., regions where the polypeptide couples or interacts with intracellular or intramembrane
5 binding partners.

After the agent has been administered in such a way that it can gain access, it can be determined whether the test agent modulates expression or biological activity. Modulation can be of any type, quality, or quantity, e.g., increase, facilitate, enhance, up-regulate, stimulate, activate, amplify, augment, induce, decrease, down-regulate, diminish, lessen, 10 reduce, etc. The modulatory quantity can also encompass any value, e.g., 1%, 5%, 10%, 50%, 75%, 1-fold, 2-fold, 5-fold, 10-fold, 100-fold, etc. To modulate expression means, e.g., that the test agent has an effect on its expression, e.g., to effect the amount of transcription, to effect RNA splicing, to effect translation of the RNA into polypeptide, to effect RNA or polypeptide stability, to effect polyadenylation or other processing of the RNA, to effect post- 15 transcriptional or post-translational processing, etc. To modulate biological activity means, e.g., that a functional activity of the polypeptide is changed in comparison to its normal activity in the absence of the agent. This effect includes, increase, decrease, block, inhibit, enhance, etc.

A test agent can be of any molecular composition, e.g., chemical compounds, 20 biomolecules, such as polypeptides, lipids, nucleic acids (e.g., antisense), carbohydrates, antibodies, ribozymes, double-stranded RNA, aptamers, etc. For example, if a polypeptide to be modulated is a cell-surface molecule, a test agent can be an antibody that specifically recognizes it and, e.g., causes the polypeptide to be internalized, leading to its down regulation on the surface of the cell. Such an effect does not have to be permanent, but can 25 require the presence of the antibody to continue the down-regulatory effect. Antibodies can also be used to modulate the biological activity of a polypeptide in a lysate or other cell-free form.

Additional cell-based test systems suitable for the analysis of GPCR polypeptides are summarized in Marchese et al. (1999, Trends in Pharmacol. Sci. 20: 370-375) and comprise 30 so-called "ligand screening assays." For example in yeast cells the pheromone receptor can be replaced by a GPCR according to the invention. The effect of test substances on the receptor

can be determined upon modulation of histidine synthesis, i.e. by growing in histidine-free medium. In addition using cells transfected with nucleic acids according to the invention it can be analyzed whether test substances mediate translocation of a detectable arrestins, for example of a arrestin-GFP-fusion protein. Moreover, it can be analyzed whether test

5 substances mediate GPCR-mediated dispersion or aggregation of *Xenopus laevis* melanophores. Another test system utilizes the universal adapter G-protein G alphal6, which mobilizes Ca.sup.2+. Other screening test systems are described in Lemer et al., *supra*; WO96/41169; U.S. Pat. No. 5,482,835; WO99/06535; EP 0 939 902; WO99/66326; WO98/34948; EP 0 863 214; U.S. Pat. No. 5,882,944 and U.S. Pat. No. 5,891,641.

10 Therapeutics

Selective polynucleotides, polypeptides, and specific-binding partners thereto, can be utilized in therapeutic applications, especially to treat diseases and conditions described herein. Useful methods include, but are not limited to, immunotherapy (e.g., using specific-binding partners to polypeptides), vaccination (e.g., using a selective polypeptide or a naked 15 DNA encoding such polypeptide), protein or polypeptide replacement therapy, gene therapy (e.g., germ-line correction, antisense), etc.

Various immunotherapeutic approaches can be used. For instance, unlabeled antibody that specifically recognizes a tissue-specific antigen can be used to stimulate the body to destroy or attack a cancer or other diseased tissue, to cause down-regulation, to 20 produce complement-mediated lysis, to inhibit cell growth, etc., of target cells which display the antigen, e.g., analogously to how c-erbB-2 antibodies are used to treat breast cancer. In addition, antibody can be labeled or conjugated to enhance its deleterious effect, e.g., with radionuclides and other energy emitting entities, toxins, such as ricin, exotoxin A (ETA), and diphtheria, cytotoxic or cytostatic agents, immunomodulators, chemotherapeutic agents; 25 etc. See, e.g., U.S. Pat. No. 6,107,090.

An antibody or other specific-binding partner can be conjugated to a second molecule, such as a cytotoxic agent, and used for targeting the second molecule to a tissue-antigen positive cell (Vitetta, E. S. et al., 1993, Immunotoxin therapy, in DeVita, Jr., V. T. et al., eds, Cancer: Principles and Practice of Oncology, 4th ed., J.B. Lippincott Co., Philadelphia, 30 2624-2636). Examples of cytotoxic agents include, but are not limited to, antimetabolites, alkylating agents, anthracyclines, antibiotics, anti-mitotic agents, radioisotopes and

chemotherapeutic agents. Further examples of cytotoxic agents include, but are not limited to ricin, doxorubicin, daunorubicin, taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, 1-dehydrotestosterone, diphtheria toxin, *Pseudomonas exotoxin (PE) A, PE40, abrin, elongation factor-2 and glucocorticoid.* Techniques for conjugating therapeutic agents to antibodies are well.

In addition to immunotherapy, polynucleotides and polypeptides can be used as targets for non-immunotherapeutic applications, e.g., using compounds which interfere with function, expression (e.g., antisense as a therapeutic agent), assembly, etc. RNA interference 10 can be used in vitro and in vivo to silence a gene when its expression contributes to a disease (but also for other purposes, e.g., to identify the gene's function to change a developmental pathway of a cell, etc.). See, e.g., Sharp and Zamore, *Science*, 287:2431-2433, 2001; Grishok et al., *Science*, 287:2494, 2001.

Delivery of therapeutic agents can be achieved according to any effective method, 15 including, liposomes, viruses, plasmid vectors, bacterial delivery systems, orally, systemically, etc. Therapeutic agents of the present invention can be administered in any form by any effective route, including, e.g., oral, parenteral, enteral, intraperitoneal, topical, transdermal (e.g., using any standard patch), intravenously, ophthalmic, nasally, local, non-oral, such as aerosol, inhalation, subcutaneous, intramuscular, buccal, sublingual, rectal, 20 vaginal, intra-arterial, and intrathecal, etc. They can be administered alone, or in combination with any ingredient(s), active or inactive.

In addition to therapeutics, *per se*, the present invention also relates to methods of treating a disease showing altered expression of a tissue selective gene, comprising, e.g., administering to a subject in need thereof a therapeutic agent which is effective for regulating 25 expression of said gene and/or which is effective in treating said disease. The term "treating" is used conventionally, e.g., the management or care of a subject for the purpose of combating, alleviating, reducing, relieving, improving the condition of, etc., of a disease or disorder. By the phrase "altered expression," it is meant that the disease is associated with a mutation in the gene, or any modification to the gene (or corresponding product) which 30 affects its normal function. Thus, expression refers to, e.g., transcription, translation, splicing, stability of the mRNA or protein product, activity of the gene product, differential

expression, etc.

Any agent which "treats" the disease can be used. Such an agent can be one which regulates the expression of a tissue selective gene. Expression refers to the same acts already mentioned, e.g. transcription, translation, splicing, stability of the mRNA or protein product, 5 activity of the gene product, differential expression, etc. For instance, if the condition was a result of a complete deficiency of the gene product, administration of gene product to a patient would be said to treat the disease and regulate the gene's expression. Many other possible situations are possible, e.g., where the gene is aberrantly expressed, and the therapeutic agent regulates the aberrant expression by restoring its normal expression pattern.

10

Antisense

Antisense polynucleotide (e.g., RNA) can also be prepared from a polynucleotide according to the present invention. Antisense polynucleotide can be used in various ways, such as to regulate or modulate expression of the polypeptides they encode, e.g., inhibit their 15 expression, for *in situ* hybridization, for therapeutic purposes, for making targeted mutations (in vivo, triplex, etc.) etc. For guidance on administering and designing anti-sense, see, e.g., U.S. Pat. Nos. 6,200,960, 6,200,807, 6,197,584, 6,190,869, 6,190,661, 6,187,587, 6,168,950, 6,153,595, 6,150,162, 6,133,246, 6,117,847, 6,096,722, 6,087,343, 6,040,296, 6,005,095, 5,998,383, 5,994,230, 5,891,725, 5,885,970, and 5,840,708. An antisense polynucleotides 20 can be operably linked to an expression control sequence. A total length of about 35 bp can be used in cell culture with cationic liposomes to facilitate cellular uptake, but for *in vivo* use, preferably shorter oligonucleotides are administered, e.g. 25 nucleotides.

Antisense polynucleotides can comprise modified, nonnaturally-occurring nucleotides and linkages between the nucleotides (e.g., modification of the phosphate-sugar backbone; 25 methyl phosphonate, phosphorothioate, or phosphorodithioate linkages; and 2'-O-methyl ribose sugar units), e.g., to enhance *in vivo* or *in vitro* stability, to confer nuclease resistance, to modulate uptake, to modulate cellular distribution and compartmentalization, etc. Any effective nucleotide or modification can be used, including those already mentioned, as known in the art, etc., e.g., disclosed in U.S. Pat. Nos. 6,133,438; 6,127,533; 6,124,445; 30 6,121,437; 5,218,103 (e.g., nucleoside thiophosphoramidites); 4,973,679; Sproat et al., "2'-O-Methyloligonucleotides: synthesis and applications," Oligonucleotides and Analogs A

Practical Approach, Eckstein (ed.), IRL Press, Oxford, 1991, 49-86; Iribarren et al., "2'-O-Alkyl Oligoribonucleotides as Antisense Probes," Proc. Natl. Acad. Sci. USA, 1990, 87, 7747-7751; Cotton et al., "2'-O-methyl, 2'-O-ethyl oligoribonucleotides and phosphorothioate oligodeoxyribonucleotides as inhibitors of the in vitro U7 snRNP-dependent mRNA processing event," Nucl. Acids Res., 1991, 19, 2629-2635.

5 Arrays

The present invention also relates to an ordered array of polynucleotide probes and specific-binding partners (e.g., antibodies) for detecting the expression of tissue selective genes or polypeptides encoded thereby, in a sample, comprising, one or more polynucleotide probes or specific binding partners associated with a solid support or in separate receptacles, wherein each probe is specific for a tissue selective gene or a specific-binding partner which is specific for a polypeptide.

The phrase "ordered array" indicates that the probes are arranged in an identifiable or position-addressable pattern, e.g., such as the arrays disclosed in U.S. Pat. Nos. 6,156,501, 6,077,673, 6,054,270, 5,723,320, 5,700,637, WO09919711, WO00023803. The probes are associated with the solid support in any effective way. For instance, the probes can be bound to the solid support, either by polymerizing the probes on the substrate, or by attaching a probe to the substrate. Association can be, covalent, electrostatic, noncovalent, hydrophobic, hydrophilic, noncovalent, coordination, adsorbed, absorbed, polar, etc. When fibers or hollow filaments are utilized for the array, the probes can fill the hollow orifice, be absorbed into the solid filament, be attached to the surface of the orifice, etc. Probes can be of any effective size, sequence identity, composition, etc., as already discussed.

25 Transgenic animals

The present invention also relates to transgenic animals comprising tissue selective genes, and homologs thereof. (Methods of making transgenic animals, and associated recombinant technology, can be accomplished conventionally, e.g., as described in *Transgenic Animal Technology*, Pinkert et al., 2nd Edition, Academic Press, 2002.) Such genes, as discussed in more detail below, include, but are not limited to, functionally-disrupted genes, mutated genes, ectopically or selectively-expressed genes, inducible or

regulatable genes, etc. These transgenic animals can be produced according to any suitable technique or method, including homologous recombination, mutagenesis (e.g., ENU, Rathkolb et al., *Exp. Physiol.*, 85(6):635-644, 2000), and the tetracycline-regulated gene expression system (e.g., U.S. Pat. No. 6,242,667). The term "gene" as used herein includes 5 any part of a gene, i.e., regulatory sequences, promoters, enhancers, exons, introns, coding sequences, etc. The nucleic acid present in the construct or transgene can be naturally occurring wild-type, polymorphic, or mutated. Where the animal is a non-human animal, its homolog can be used instead. Transgenic animals can have structural and/or functional defects in any of the tissues described herein, e.g., pancreas, kidney, retina, and immune cells, 10 as well as having or being susceptible to any of the associated disorders or diseases mentioned herein.

Along these lines, polynucleotides of the present invention can be used to create transgenic animals, e.g. a non-human animal, comprising at least one cell whose genome comprises a functional disruption of one or tissue selective genes, or homologs thereof (e.g., 15 a mouse homolog when a mouse is used). By the phrases "functional disruption" or "functionally disrupted," it is meant that the gene does not express a biologically-active product. It can be substantially deficient in at least one functional activity coded for by the gene. Expression of a polypeptide can be substantially absent, i.e., essentially undetectable amounts are made. However, polypeptide can also be made, but which is deficient in 20 activity, e.g., where only an amino-terminal portion of the gene product is produced.

The transgenic animal can comprise one or more cells. When substantially all its cells contain the engineered gene, it can be referred to as a transgenic animal "whose genome comprises" the engineered gene. This indicates that the endogenous gene loci of the animal has been modified and substantially all cells contain such modification.

25 Functional disruption of the gene can be accomplished in any effective way, including, e.g., introduction of a stop codon into any part of the coding sequence such that the resulting polypeptide is biologically inactive (e.g., because it lacks a catalytic domain, a ligand binding domain, etc.), introduction of a mutation into a promoter or other regulatory sequence that is effective to turn it off, or reduce transcription of the gene, insertion of an 30 exogenous sequence into the gene which inactivates it (e.g., which disrupts the production of a biologically-active polypeptide or which disrupts the promoter or other transcriptional

machinery), deletion of sequences from the gene (or homolog thereof), etc. Examples of transgenic animals having functionally disrupted genes are well known, e.g., as described in U.S. Pat. Nos. 6,239,326, 6,225,525, 6,207,878, 6,194,633, 6,187,992, 6,180,849, 6,177,610, 6,100,445, 6,087,555, 6,080,910, 6,069,297, 6,060,642, 6,028,244, 6,013,858, 5,981,830, 5,866,760, 5,859,314, 5,850,004, 5,817,912, 5,789,654, 5,777,195, and 5,569,824. A transgenic animal which comprises the functional disruption can also be referred to as a "knock-out" animal, since the biological activity of its gene has been "knocked-out." Knock-outs can be homozygous or heterozygous.

For creating functionally disrupted genes, and other gene mutations, homologous recombination technology is of special interest since it allows specific regions of the genome to be targeted. Using homologous recombination methods, genes can be specifically-inactivated, specific mutations can be introduced, and exogenous sequences can be introduced at specific sites. These methods are well known in the art, e.g., as described in the patents above. See, also, Robertson, *Biol. Reproduc.*, 44(2):238-245, 1991. Generally, the genetic engineering is performed in an embryonic stem (ES) cell, or other pluripotent cell line (e.g., adult stem cells, EG cells), and that genetically-modified cell (or nucleus) is used to create a whole organism. Nuclear transfer can be used in combination with homologous recombination technologies. For example, a gene locus can be disrupted in mouse ES cells using a positive-negative selection method (e.g., Mansour et al., *Nature*, 336:348-352, 1988).

In this method, a targeting vector can be constructed which comprises a part of the gene to be targeted. A selectable marker, such as neomycin resistance genes, can be inserted into a exon present in the targeting vector, disrupting it. When the vector recombines with the ES cell genome, it disrupts the function of the gene. The presence in the cell of the vector can be determined by expression of neomycin resistance. See, e.g., U.S. Pat. No. 6,239,326.

Cells having at least one functionally disrupted gene can be used to make chimeric and germline animals, e.g., animals having somatic and/or germ cells comprising the engineered gene. Homozygous knock-out animals can be obtained from breeding heterozygous knock-out animals. See, e.g., U.S. Pat. No. 6,225,525.

The present invention also relates to non-human, transgenic animal whose genome comprises recombinant tissue selective nucleic acid (and homologs thereof) operatively linked to an expression control sequence effective to express said coding sequence in a target

tissue. Such a transgenic animal can also be referred to as a "knock-in" animal since an exogenous gene has been introduced, stably, into its genome. "Operable linkage" has the meaning used through the specification, i.e., placed in a functional relationship with another nucleic acid. When a gene is operably linked to an expression control sequence, as explained 5 above, it indicates that the gene (e.g., coding sequence) is joined to the expression control sequence (e.g., promoter) in such a way that facilitates transcription and translation of the coding sequence. As described above, the phrase "genome" indicates that the genome of the cell has been modified. In this case, the recombinant gene has been stably integrated into the genome of the animal. The nucleic acid (e.g., a coding sequence) in operable linkage with 10 the expression control sequence can also be referred to as a construct or transgene.

Any expression control sequence can be used depending on the purpose. For instance, if selective expression is desired, then expression control sequences which limit its expression can be selected. These include, e.g., tissue or cell-specific promoters, introns, enhancers, etc. For various methods of cell and tissue-specific expression, see, e.g., U.S. Pat. 15 Nos. 6,215,040, 6,210,736, and 6,153,427. These also include the endogenous promoter, i.e., the coding sequence can be operably linked to its own promoter. Inducible and regulatable promoters can also be utilized.

The present invention also relates to a transgenic animal which contains a functionally disrupted and a transgene stably integrated into the animals genome. Such an animal can be 20 constructed using combinations any of the above- and below-mentioned methods. Such animals have any of the aforementioned uses, including permitting the knock-out of the normal gene and its replacement with a mutated gene. Such a transgene can be integrated at the endogenous gene locus so that the functional disruption and "knock-in" are carried out in the same step.

25 In addition to the methods mentioned above, transgenic animals can be prepared according to known methods, including, e.g., by pronuclear injection of recombinant genes into pronuclei of 1-cell embryos, incorporating an artificial yeast chromosome into embryonic stem cells, gene targeting methods, embryonic stem cell methodology, cloning methods, nuclear transfer methods. See, also, e.g., U.S. Patent Nos. 4,736,866; 4,873,191; 30 4,873,316; 5,082,779; 5,304,489; 5,174,986; 5,175,384; 5,175,385; 5,221,778; Gordon et al., Proc. Natl. Acad. Sci., 77:7380-7384, 1980; Palmiter et al., Cell, 41:343-345, 1985; Palmiter

et al., Ann. Rev. Genet., 20:465-499, 1986; Askew et al., Mol. Cell. Bio., 13:4115-4124, 1993; Games et al. Nature, 373:523-527, 1995; Valancius and Smithies, Mol. Cell. Bio., 11:1402-1408, 1991; Stacey et al., Mol. Cell. Bio., 14:1009-1016, 1994; Hasty et al., Nature, 350:243-246, 1995; Rubinstein et al., Nucl. Acid Res., 21:2613-2617, 1993; Cibelli et al., 5 Science, 280:1256-1258, 1998. For guidance on recombinase excision systems, see, e.g., U.S. Pat. Nos. 5,626,159, 5,527,695, and 5,434,066. See also, Orban, P.C., et al., "Tissue- and Site-Specific DNA Recombination in Transgenic Mice," Proc. Natl. Acad. Sci. USA, 89:6861-6865 (1992); O'Gorman, S., et al., "Recombinase-Mediated Gene Activation and Site-Specific Integration in Mammalian Cells," Science, 251:1351-1355 (1991); Sauer, B., et 10 al., "Cre-stimulated recombination at loxP-Containing DNA sequences placed into the mammalian genome," Polynucleotides Research, 17(1):147-161 (1989); Gagneten, S. et al. (1997) Nucl. Acids Res. 25:3326-3331; Xiao and Weaver (1997) Nucl. Acids Res. 25:2985-2991; Agah, R. et al. (1997) J. Clin. Invest. 100:169-179; Barlow, C. et al. (1997) Nucl. Acids Res. 25:2543-2545; Araki, K. et al. (1997) Nucl. Acids Res. 25:868-872; Mortensen, 15 R. N. et al. (1992) Mol. Cell. Biol. 12:2391-2395 (G418 escalation method); Lakhani, P. P. et al. (1997) Proc. Natl. Acad. Sci. USA 94:9950-9955 ("hit and run"); Westphal and Leder (1997) Curr. Biol. 7:530-533 (transposon-generated "knock-out" and "knock-in"); Templeton, N. S. et al. (1997) Gene Ther. 4:700-709 (methods for efficient gene targeting, allowing for a high frequency of homologous recombination events, e.g., without selectable 20 markers); PCT International Publication WO 93/22443 (functionally-disrupted).

A polynucleotide according to the present invention can be introduced into any non-human animal, including a non-human mammal, mouse (Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1986), pig (Hammer et al., Nature, 315:343-345, 1985), sheep (Hammer et al., 25 Nature, 315:343-345, 1985), cattle, rat, or primate. See also, e.g., Church, 1987, Trends in Biotech. 5:13-19; Clark et al., Trends in Biotech. 5:20-24, 1987); and DePamphilis et al., BioTechniques, 6:662-680, 1988. Transgenic animals can be produced by the methods described in U.S. Pat. No. 5,994,618, and utilized for any of the utilities described therein.

30 Database

The present invention also relates to electronic forms of polynucleotides,

polypeptides, etc., of the present invention, including computer-readable medium (e.g., magnetic, optical, etc., stored in any suitable format, such as flat files or hierarchical files) which comprise such sequences, or fragments thereof, e-commerce-related means, etc.

Along these lines, the present invention relates to methods of retrieving nucleic acid and/or 5 polypeptide sequences from a computer-readable medium, comprising, one or more of the following steps in any effective order, e.g., selecting a cell or gene expression profile, e.g., a profile that specifies that said gene is differentially expressed in a tissue as described herein, and retrieving said differentially expressed nucleic acid or polypeptide.

A "gene expression profile" means the list of tissues, cells, etc., in which a defined 10 gene is expressed (i.e, transcribed and/or translated). A "cell expression profile" means the genes which are expressed in the particular cell type. The profile can be a list of the tissues in which the gene is expressed, but can include additional information as well, including level of expression (e.g., a quantity as compared or normalized to a control gene), and information on temporal (e.g., at what point in the cell-cycle or developmental program) and 15 spatial expression. By the phrase "selecting a gene or cell expression profile," it is meant that a user decides what type of gene or cell expression pattern he is interested in retrieving, e.g., he may require that the gene is differentially expressed in a tissue, or he may require that the gene is not expressed in blood, but must be expressed in pancreas. Any pattern of expression preferences may be selected. The selecting can be performed by any effective method. In 20 general, "selecting" refers to the process in which a user forms a query that is used to search a database of gene expression profiles. The step of retrieving involves searching for results in a database that correspond to the query set forth in the selecting step. Any suitable algorithm can be utilized to perform the search query, including algorithms that look for matches, or that perform optimization between query and data. The database is information that has been 25 stored in an appropriate storage medium, having a suitable computer-readable format. Once results are retrieved, they can be displayed in any suitable format, such as HTML.

For instance, the user may be interested in identifying genes that are differentially expressed in a pancreas or kidney. He may not care whether small amounts of expression occur in other tissues, as long as such genes are not expressed in peripheral blood 30 lymphocytes. A query is formed by the user to retrieve the set of genes from the database

having the desired gene or cell expression profile. Once the query is inputted into the system, a search algorithm is used to interrogate the database, and retrieve results.

Advertising, licensing, etc., methods

5 The present invention also relates to methods of advertising, licensing, selling, purchasing, brokering, etc., genes, polynucleotides, specific-binding partners, antibodies, etc., of the present invention. Methods can comprises, e.g., displaying tissue selective polynucleotide or polypeptide sequences, or antibody specific thereto, in a printed or computer-readable medium (e.g., on the Web or Internet), accepting an offer to purchase said
10 gene, polypeptide, or antibody.

Other

A polynucleotide, probe, polypeptide, antibody, specific-binding partner, etc., according to the present invention can be isolated. The term "isolated" means that the
15 material is in a form in which it is not found in its original environment or in nature, e.g., more concentrated, more purified, separated from component, etc. An isolated polynucleotide includes, e.g., a polynucleotide having the sequenced separated from the chromosomal DNA found in a living animal, e.g., as the complete gene, a transcript, or a cDNA. This polynucleotide can be part of a vector or inserted into a chromosome (by
20 specific gene-targeting or by random integration at a position other than its normal position) and still be isolated in that it is not in a form that is found in its natural environment. A polynucleotide, polypeptide, etc., of the present invention can also be substantially purified. By substantially purified, it is meant that polynucleotide or polypeptide is separated and is essentially free from other polynucleotides or polypeptides, i.e., the polynucleotide or
25 polypeptide is the primary and active constituent. A polynucleotide can also be a recombinant molecule. By "recombinant," it is meant that the polynucleotide is an arrangement or form which does not occur in nature. For instance, a recombinant molecule comprising a promoter sequence would not encompass the naturally-occurring gene, but would include the promoter operably linked to a coding sequence not associated with it in
30 nature, e.g., a reporter gene, or a truncation of the normal coding sequence.

The term "marker" is used herein to indicate a means for detecting or labeling a target. A marker can be a polynucleotide (usually referred to as a "probe"), polypeptide (e.g., an antibody conjugated to a detectable label), PNA, or any effective material.

5 The topic headings set forth above are meant as guidance where certain information can be found in the application, but are not intended to be the only source in the application where information on such topic can be found. Reference materials

For other aspects of the polynucleotides, reference is made to standard textbooks of molecular biology. See, e.g., Hames et al., Polynucleotide Hybridization, IL Press, 1985; Davis et al., Basic Methods in Molecular Biology, Elsevier Sciences Publishing, Inc., New York, 1986; Sambrook et al., Molecular Cloning, CSH Press, 1989; Howe, Gene Cloning and Manipulation, Cambridge University Press, 1995; Ausubel et al., Current Protocols in Molecular Biology, John Wiley & Sons, Inc., 1994-1998.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following 15 preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever. The entire disclosure of all applications, patents and publications, cited above and in the figures are hereby incorporated by reference in their entirety, including U.S. Application Serial Nos. 60/372,669 April 16, 2003, 60/374,823 filed April 24, 2002, 60/376,558 filed May 1, 2002, 60/381,366 20 filed May 20, 2002, 60/403,648 filed August 16, 2002, 60/411,882 filed September 20, 2002, and 60/424,336 filed November 7, 2002.

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TABLE 1

| Clone ID (gene code) | ACCN | Predominant sites of expression | Other expression sites | Cytogenetic band |
|----------------------|-----------|---------------------------------|-------------------------|------------------|
| TMD0024 | XM_060945 | thymus | none | 1q22 |
| TMD1779 | XM_060946 | thymus and PBL | none | 1q22 |
| TMD0884 | XM_060947 | thymus | skin and ovary | 1q22 |
| TMD0025 | XM_060948 | thymus | none | 1q22 |
| TMD1780 | XM_089422 | thymus | none | 1q22 |
| TMD1781 | XM_089421 | PBL | thymus | 1q22 |
| TMD0304 | XM_060956 | bone marrow and muscle | testis | 1q22 |
| TMD0888 | XM_060957 | bone marrow | lung, muscle and testis | 1q22 |
| TMD0890 | XM_060959 | bone marrow | lung and PBL | 1q22 |

TABLE 2

5

| Clone ID (gene code) | ACCN | Protein seq length | Domain Description |
|----------------------|-----------|--------------------|---|
| TMD1779 | XM_060946 | 264 | Transmembrane domain: 26 - 48 Transmembrane domain: 55 - 77 Transmembrane domain: 92 - 114 Transmembrane domain: 134 - 156 Transmembrane domain: 197 - 219 |
| TMD0024 | XM_060945 | 268 | Transmembrane domain: 16 - 38 Transmembrane domain: 53 - 75 Transmembrane domain: 96 - 118 Transmembrane domain: 156 - 178 Transmembrane domain: 191 - 213 Transmembrane domain: 228 - 246 |
| TMD0025 | XM_060948 | 313 | Transmembrane domain: 29 - 51 Transmembrane domain: 58 - 77 Transmembrane domain: 92 - 114 Transmembrane domain: 135 - 157 Transmembrane domain: 197 - 219 Transmembrane domain: 240 - 262 Transmembrane domain: 272 - 294 |
| TMD0304 | XM_060956 | 319 | Transmembrane domain: 28 - 50 Transmembrane domain: 63 - 82 Transmembrane domain: 102 - 124 Transmembrane domain: 144 - 166 Transmembrane domain: 205 - 227 Transmembrane domain: 240 - 262 Transmembrane domain: 272 - 294 |
| TMD0884 | XM_060947 | 299 | Transmembrane domain: 20 - 42 Transmembrane domain: 54 - 76 Transmembrane domain: 91 - 113 Transmembrane domain: 126 - 148 |

| | | | | |
|----|---------|-----------|-----|--|
| | | | | Transmembrane domain: 183 - 205 Transmembrane domain: 226 - 248 Transmembrane domain: 258 - 277 |
| 5 | TMD0888 | XM_060957 | 312 | Transmembrane domain: 25 - 47 Transmembrane domain: 59 - 78 Transmembrane domain: 98 - 120 Transmembrane domain: 141 - 163 Transmembrane domain: 207 - 229 Transmembrane domain: 241 - 260 Transmembrane domain: 270 - 292 |
| 10 | | | | |
| 15 | TMD0890 | XM_060959 | 280 | Transmembrane domain: 26 - 48 Transmembrane domain: 122 - 144 Transmembrane domain: 180 - 202 Transmembrane domain: 215 - 237 Transmembrane domain: 252 - 269 |
| 20 | TMD1780 | XM_089422 | 491 | Transmembrane domain: 20 - 42 Transmembrane domain: 54 - 76 Transmembrane domain: 91 - 113 Transmembrane domain: 137 - 159 Transmembrane domain: 190 - 212 Transmembrane domain: 231 - 253 Transmembrane domain: 266 - 283 Transmembrane domain: 304 - 326 Transmembrane domain: 336 - 358 Transmembrane domain: 379 - 401 Transmembrane domain: 437 - 459 |
| 25 | | | | |
| 30 | TMD1781 | XM_089421 | 91 | Transmembrane domain: 63 - 85 |
| 35 | | | | |

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| | TMD0024 XM_060945 | TMD1779 XM_060946 | TMD0884 XM_060947 | TMD0025 XM_060948 | TMD1780 XM_089422 | TMD1781 XM_089421 | TMD0304 XM_060956 | TMD0888 XM_060957 |
|----------------------|---|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|----------------------|
| TMD0024 XM_060945 | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1779 XM_060946 | no significant similarity | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0884 XM_060947 | 74% (37nt) | no significant similarity | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0025 XM_060948 | 71% (222nt) 80% (73nt) | 90% (605nt) | 83% (34nt) | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1780 XM_089422 | 81% (114nt) 74% (186nt) 79% (113nt) 77% (90nt) | 83% (71nt) | 78% (90nt) | [REDACTED] | 80% (84nt) | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1781 XM_089421 | 91% (35nt) 77% (80nt) | no significant similarity | no significant similarity | no significant similarity | 77% (179nt) 82% (46nt) | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0304 XM_060956 | no significant similarity | no significant similarity | no significant similarity | no significant similarity | 84% (39nt) | no significant similarity | [REDACTED] | [REDACTED] |
| TMD0888 XM_060957 | no significant similarity | no significant similarity | no significant similarity | 84% (38nt) | no significant similarity | no significant similarity | 73% (241nt) | [REDACTED] |
| TMD0890 XM_060959 | no significant similarity | no significant similarity | no significant similarity | no significant similarity | no significant similarity | no significant similarity | no significant similarity | 84% (39nt) |

TABLE 3

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| | TMD0024 XP_060945 | TMD1779 XP_060946 | TMD0884 XP_060947 | TMD0025 XP_060948 | TMD1780 XP_089422 | TMD1781 XP_089421 | TMD0304 XP_060956 | TMD0888 XP_060957 |
|----------------------|----------------------------|----------------------------|----------------------------|----------------------|----------------------------|----------------------|----------------------|----------------------|
| TMD0024 XP_060945 | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1779 XP_060946 | 47% (200aa) | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0884 XP_060947 | 62% (171aa) | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0025 XP_060948 | 53% (252aa) | 73% (233aa) | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1780 XP_089422 | 59% (261aa) 59% (181aa) | 46% (227aa) 46% (169aa) | 55% (165aa) 47% (111aa) | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD1781 XP_089421 | 40% (94aa) | 33% (82aa) | 52% (40aa) | 37% (94aa) | 51% (93aa) 49% (77aa) | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0304 XP_060956 | 40% (257aa) | 37% (229aa) | 36% (163aa) | 39% (299aa) | 39% (300aa) | [REDACTED] | [REDACTED] | [REDACTED] |
| TMD0888 XP_060957 | 49% (251aa) | 37% (239aa) | 41% (157aa) | 40% (305aa) | 45% (304aa) 43% (189aa) | 41% (82aa) | 50% (301aa) | [REDACTED] |
| TMD0890 XP_060959 | 41% (196) | 32% (132aa) | 32% (156aa) | 36% (179aa) | 42% (200aa) | 38% (72aa) | 36% (196aa) | 46% (196aa) |

TABLE 4

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| ციტონები | სრული დოკუმენტი | სრული დოკუმენტი |
|------------------------------|---|---|
| TMD1779 (SEQ ID NO 1-2) | GGTCAATGAGACTGG TGAGAGGTCTCT (SEQ ID NO 3) | CTACATCCCGATGG GAAACTGAG (SEQ ID NO 4) |
| TMD0024 (SEQ ID NO 6-7) | CCACCTGCTCTCAGACA CCAAGACC (SEQ ID NO 8) | GGCACCATATACTCAGGAT GCTGAGG (SEQ ID NO 9) |
| TMD0025 (SEQ ID NO 12-13) | CCTGTTCACTCTGGCA CCAATGCC (SEQ ID NO 14) | CTGGTTGGAGGTGGAG GGCAG (SEQ ID NO 15) |
| TMD0034 (SEQ ID NO 20-21) | CTCTATGTTCCGCATGC GCACAG (SEQ ID NO 22) | GCAAGGGGGAAAATCCATGC ATCTCAG (SEQ ID NO 23) |
| TMD0084 (SEQ ID NO 25-26) | TGTCAATATCCTGGTGT CAGTGGCTCC (SEQ ID NO 27) | CATCTAACCGAGAACCTTCT CAGAGCCTC (SEQ ID NO 28) |
| TMD0088 (SEQ ID NO 33-34) | GGAACTGGAGCCAGGA GCAGATTCTAC (SEQ ID NO 35) | GGAGAAGGGATCAGCAGG AAGCTG (SEQ ID NO 36) |
| TMD0090 (SEQ ID NO 40-41) | TCAACCACTGGACC CTACAACT (SEQ ID NO 42) | GGCCACACCAATCACTGTGC CAT (SEQ ID NO 43) |
| TMD1780 (SEQ ID NO 47-48) | CCTGAAATCTCAAC AACTGTTATTCTGCCCA (SEQ ID NO 49) | ATGAGATGGAAAGCACAGGT GGAGAG (SEQ ID NO 50) |
| TMD1781 (SEQ ID NO 55-56) | ATGACAGTTATGATTC TATGTTGCCATCTGC (SEQ ID NO 57) | TCAGGATGGTGTGAAATG AAGCCATAG (SEQ ID NO 58) |

TABLE 5

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TABLE 6

| SEQ ID NO | GENE NUMBER | GENBANK IDENTIFIER | PREDOMINANT SITES OF EXPRESSION | PROMOTER (SEQ ID NO) | PRIMER (FOR, REV) (SEQ ID NO) |
|-----------|-------------|--------------------|---------------------------------|----------------------|-------------------------------|
| 63,64 | TMD0785 | XM_060310 | kidney | 65-68 | 69,70 |

| | XM_062147 | XM_061676 |
|---------|-----------|-----------|
| outside | 1-27 | 1-28 |
| TM(1) | 28-50 | 29-51 |
| inside | 51-61 | 52-62 |
| TM(2) | 62-84 | 63-85 |
| outside | 85-98 | 86-99 |
| TM(3) | 99-121 | 100-122 |
| inside | 122-140 | 123-133 |
| TM(4) | 141-163 | 134-156 |
| outside | 164-203 | 157-201 |
| TM(5) | 204-226 | 202-224 |
| inside | 227-237 | 225-236 |
| TM(6) | 238-260 | 237-259 |
| outside | 261-274 | 260-273 |
| TM(7) | 275-293 | 274-296 |
| inside | 294-313 | 297-314 |

TABLE 7

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| Clone ID (genecode) | ACCN | Gene Name/Description | Predominant sites of expression | Other expression sites |
|---------------------|-----------|--|-------------------------------------|---|
| TMD0049 | XM_057351 | Homo sapiens similar to organic anion transporter 4 like protein (LOC116085) mRNA | kidney | none |
| TMD0190 | XM_087157 | Homo sapiens similar to sodium-coupled ascorbic acid transporter 2 (LOC151295) mRNA | kidney | colon and liver |
| TMD0242 | XM_088369 | Homo sapiens similar to unnamed protein product (LOC157724) mRNA | kidney | none |
| TMD0335 | XM_089360 | Homo sapiens similar to sodium iodide symporter (LOC159963) mRNA | kidney | adrenal gland, heart, intestine(small), liver, muscle, testis |
| TMD0371 (new) | XM_089732 | Homo sapiens similar to CG8271 gene product (LOC196023) mRNA | kidney | pancreas and testis |
| TMD0374 (new) | XM_085595 | Homo sapiens similar to unnamed protein product (LOC146802) mRNA | kidney, muscle, ovary, skin, testis | |
| TMD0469 | XM_038736 | Homo sapiens solute carrier family 4 sodium bicarbonate cotransporter member 9 (SLC4A9) mRNA | kidney | none |
| TMD0719 | XM_059348 | Homo sapiens hypothetical gene supported by XM_059548 (LOC131920) mRNA | kidney | none |
| TMD0731 | XM_059703 | Homo sapiens similar to putative (H. sapiens) (LOC34288) mRNA | kidney | adrenal gland, muscle, thyroid |
| TMD0785 | XM_060310 | Homo sapiens similar to olfactory receptor MOR275-2 (LOC127059) mRNA | kidney | none |
| TMD0841 | XM_060823 | Homo sapiens similar to KIAA0711 gene product (H. sapiens) (LOC127707) mRNA | kidney | lung |
| TMD1114 | NM_019841 | Homo sapiens transient receptor potential cation channel subfamily V member 5 (TRPV5) mRNA | kidney | none |
| TMD1148 | XM_087108 | Homo sapiens similar to calcium channel voltage-dependent gamma subunit 6 (LOC151151) mRNA | kidney | none |

TABLE 8

TABLE 9

| Gene Code | स्क्रिप्ट ID Protein सेलेक्टन नंबर(आ) | Chromatin व्हिस्यूलेशन |
|-----------|--|--|
| TMD0049 | 2 | 332 |
| | | Sugar (and other) transporter: 2 - 302 |
| | | Transmembrane domain: 12 - 34 |
| | | Transmembrane domain: 39 - 58 |
| | | Transmembrane domain: 131 - 153 |
| | | Transmembrane domain: 157 - 179 |
| | | Transmembrane domain: 186 - 205 |
| | | Transmembrane domain: 215 - 237 |
| TMD0190 | 4 | 243 |
| | | Permease family: 91 - 224 |
| TMD0242 | 6 | 470 |
| | | AA-permease: 27 - 356 |
| | | Transmembrane domain: 13 - 35 |
| | | Transmembrane domain: 50 - 72 |
| | | Transmembrane domain: 93 - 115 |
| | | Transmembrane domain: 137 - 154 |
| | | Transmembrane domain: 161 - 183 |
| | | Transmembrane domain: 207 - 229 |
| | | Transmembrane domain: 242 - 264 |
| | | Transmembrane domain: 286 - 308 |
| | | Transmembrane domain: 335 - 357 |
| | | Transmembrane domain: 362 - 379 |
| | | Transmembrane domain: 392 - 414 |
| | | Transmembrane domain: 420 - 442 |

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| | | | |
|---------|----|-----|---|
| TMD0335 | 8 | 178 | Sodium solute symporter family: 41 - 172 |
| TMD0371 | 10 | 516 | Transmembrane domain: 45 - 67 Transmembrane domain: 87 - 109 Transmembrane domain: 116 - 138 Transmembrane domain: 143 - 165 Transmembrane domain: 174 - 196 Transmembrane domain: 201 - 223 Transmembrane domain: 283 - 305 Transmembrane domain: 320 - 339 Transmembrane domain: 351 - 370 Transmembrane domain: 375 - 397 Transmembrane domain: 404 - 426 Transmembrane domain: 441 - 463 |
| TMD0374 | 12 | 566 | Transmembrane domain: 31 - 53 Transmembrane domain: 68 - 90 Transmembrane domain: 116 - 138 Transmembrane domain: 153 - 171 Transmembrane domain: 184 - 206 Transmembrane domain: 211 - 233 Transmembrane domain: 254 - 273 Transmembrane domain: 288 - 310 Transmembrane domain: 331 - 353 Transmembrane domain: 373 - 395 Transmembrane domain: 404 - 426 Transmembrane domain: 431 - 453 Transmembrane domain: 542 - 564 |

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| | | | |
|---------|----|------|--|
| TMD0469 | 14 | 983 | HCO3- transporter family: 108 - 891 Transmembrane domain: 413 - 435 Transmembrane domain: 447 - 469 Transmembrane domain: 498 - 520 Transmembrane domain: 532 - 554 Transmembrane domain: 623 - 645 Transmembrane domain: 665 - 684 Transmembrane domain: 712 - 731 Transmembrane domain: 751 - 773 Transmembrane domain: 813 - 832 Transmembrane domain: 839 - 858 Transmembrane domain: 897 - 919 |
| TMD0719 | 16 | 146 | Transmembrane domain: 7 - 29 Transmembrane domain: 49 - 71 |
| TMD0731 | 18 | 218 | Transmembrane domain: 38 - 60 Transmembrane domain: 70 - 92 |
| TMD0785 | 20 | 312 | 7 transmembrane receptor (rhodopsin family): 58 - 290 Transmembrane domain: 29 - 51 Transmembrane domain: 61 - 83 Transmembrane domain: 140 - 162 Transmembrane domain: 197 - 219 Transmembrane domain: 240 - 262 Transmembrane domain: 272 - 294 |
| TMD0841 | 22 | 1161 | Kelch motif: 850 - 895 Kelch motif: 897 - 938 |
| | | | |
| | | | |
| | | | |
| | | | |

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| | | | |
|---------|----|-----|--|
| TMD1114 | 24 | 729 | Transmembrane domain: 327 - 349 Transmembrane domain: 383 - 405 |
| | | | Transmembrane domain: 420 - 438 |
| | | | Transmembrane domain: 451 - 473 |
| | | | Transmembrane domain: 493 - 512 |
| | | | Transmembrane domain: 519 - 541 |
| | | | Transmembrane domain: 554 - 576 |
| TMD1148 | 26 | 103 | Transmembrane domain: 7 - 24 |
| | | | Transmembrane domain: 39 - 61 |
| | | | Transmembrane domain: 68 - 90 |

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| Clone ID (gene code) | Accession | Chromosome | Disease linked |
|----------------------|-----------|------------|--|
| TMD0049 | XM_057351 | 11q12.1 | osteoporosis; pseudoglioma syndrome; spastic paraplegia 17 |
| TMD0180 | XM_087157 | 2q36.2 | none |
| TMD0242 | XM_088369 | 8q21.2 | none |
| TMD0335 | XM_089960 | 11p14.2 | none |
| TMD0371A | XM_089732 | 10q23.33 | epilepsy, partial, with auditory features; spastic paraplegia 9, autosomal dominant |
| TMD0374 | XM_085595 | 17p11.2 | smith-magenis syndrome |
| TMD0469 | XM_038736 | 5q31 | paget disease of bone 4 |
| TMD0719 | XM_059548 | 3q29 | none |
| TMD0731 | XM_059703 | 5q13.2 | spastic paraplegia 11, autosomal recessive; corpus callosum, agenesis of, with neuropathy |
| TMD0785 | XM_060310 | 1q44-tel | familial cold urticaria (FCU); Muckle-Wells syndrome (MWS); prostate cancer susceptibility |
| | | | breast cancer, ductal, 2; |
| | | | prostate cancer/brain cancer susceptibility; |
| | | | melanoma, cutaneous |
| | | | glaucoma 1, open angle, f |
| TMD0841 | XM_060623 | 1p36.13 | motor neuronopathy, distal hereditary, with vocal cord paralysis; cardiomyopathy, |
| TMD1114 | NM_019841 | 7q35 | dilated, h |
| TMD1148 | XM_087108 | 2q14.1 | |

TABLE 10

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| લેટેડ (SEQ ID No) | શાલોસ (SEQ ID No) | ફ્રોન્ટલેડ (SEQ ID No) |
|-----------------------|---|--|
| TMD0049 (78, 79) | GCGCTTCGGACCTGTATCCAC (104) CAAGCTGGTCTGGGAGAAG (105) | AAGAGGCCCTAAAGAGGGTCCAGACTAACAGGAGCTRACTGAAAATA (106) |
| TMD1190 (80, 81) | ACCATCCTGCAAACTGGATGGC (107) AAGGAGCCGGAGACGGAGG (108) | GCTTTATGTTATGAAAAACCCTTTATCTGAGCCTAGAACCTGTTTGCABAATTTCGCCATAT (109) AGTGATAGTTTAATGGAGGGATAAACCTGTTGCA (110) |
| TMD242 (82, 83) | GAGCTCCCTGCGTGGCTG (111) AAGTGTAAAGGATGCCCGCTGA (112) | AGTCCCAGCTTAAAGAGACAGACAGAGAGAGAGAGAGAGAGAGAG (113) TTAGTGTTTAARAAATGTAAGAGAGAGAGAGCTAACGGAGTAAAGGA (114) |
| TMD335 (84, 85) | GTTCGCTATGGTGCACGGTATC (115) AGTCCTGGCAGTCIGGATGTG (116) | GATACAAATTAATAAAGCCAGTTAAAGTAAATATTAAGACCAAG (117) ATCTCACGATTAARATGCTGAGGTGTAAATTGTTATCATCTATGT (118) |
| TMD371 (86, 87) | CAGGATTACGGACAAACGGATGG (119) TGGGAGGCAGAGATAGCAGGCC (120) | CTAGACTTTTAAACCCCTGGTTGCACAGTGGCTCAAGCTGTAA (121) |
| TMD0374 (88, 89) | CTGGTCTGGGACCCCTATAAAGC (122) CCCCGGTCTGTTGCACTGCCTC (123) | AGCTGTCCTCATTTAAAGTGAACCTGGAGTGGATGTTCTGCTCAT (124) CGAATTCCTGAAAAACGGGAGTCACTGGGGCACCATACGCCGGGT (125) |
| TMD0469 (90, 91) | CTGGGTGTCCCTCCAAAGCAGGT (126) TACGGCCGAGAGGACTGGATG (127) | TAACAAATACATAATGAGGAGTTACTAGTAGTGTACTGTAGGAA (128) ACTRAAAATAATAAAATCAGGAGGCCCTGGCACATGCTGAATCTC (129) |
| TMD0719 (92, 93) | GTACCTCTGGATCTAACGATAAGG (131) TGGGCAAGGAAAGGATAGGTAGGG (132) | GGATGCAATTAAATGCAAAACGGCCAGGGCCCCCTGGCTTCAAACCT (130) ATATACCTTGTAAAGGGGTATTATCACAAATAACAGGAAGCT (133) |
| TMD0731 (94, 95) | GGGGGGAAAGGAAAGGGAGAG (135) CCAGCTTGGATCTGGCAG (136) | ACCCCTACTTTTAAGGCTTGCACAAACAGTGTAAAGTCTCACCTTAA (134) TTATTGGGATAAAATGAAAGAGGGTCCAGAGTGTCCCTAGGTCT (137) |
| TMD0785 (96, 97) | CTTTGGGAATCTTCAGGATCACAC (138) ATGGAGGTTCGACGTCAAGCA (139) | AGGAATTGTTAAACTGGATTACTTTATCTTGTCTGTC (140) ACTTTAAATTATAAGAAGGTTCACATCAAGAAATTCCAGTGGGTT (141) |
| TMD0841 (98, 99) | GGCCACATCCACAGAGGAAGC (142) TGGCTGAGAGTAGTCCACATAGTAGCT (143) | AGGGCTTCTTCAAAAAGGGCTTGTGTTGGCCAGAAAATCAGAGTG (144) |
| TMD1114 (100, 101) | CTTCCTTCTGGTCAGAGAACAGCTGGGAC (145) GTGATGTCGAGAATGAGTGGGTTG (146) | CAGCGAGGAGAAAATGTCCTCAAGTTGAGCCCTCCCACTCCCTG (147) TAATATAAAATATATAAAATAGTGCACASATACTTATTCTCTGGTGT (148) |
| TMD1148 (102, 103) | GCAGATGACCCGACCTGACTGTTCTC (149) TGGCTGTGCAAGCTGCTGACCAAG (150) | GCAGAGAGCTTAAATGAAGGCCCTACTTGGGGAGGGAGGAAAC (151) |

TABLE 11

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| SEQ ID NO | GENE NUMBER | GENBANK IDENTIFIER | PREDOMINANT SITES OF EXPRESSION | OTHER SITES OF EXPRESSION | PROMOTER (SEQ ID NO) | PRIMER (FOR, REV) (SEQ ID NO) |
|-----------|-------------|--------------------|---------------------------------|---------------------------|----------------------|-------------------------------|
| 152, 153 | TMD0986 | XM_061779 | pancreas | low levels in testis | 156-161 | 154,155 |
| 162, 163 | TMD0987 | XM_061780 | pancreas | low levels in testis | 166 | 164,165 |
| 167, 168 | TMD0353 | XM_061781 | pancreas | | | 169,170 |
| 171, 172 | TMD0989 | XM_061784 | pancreas | | | 173,174 |
| 175, 176 | TMD058 | XM_061785 | pancreas | low levels in testis | 179,180 | 177,178 |

TABLE 12

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| | XM_061779 | XM_061780 | XM_061781 | XM_061784 | XM_061785 |
|----------------|------------------|------------------|------------------|------------------|------------------|
| outside | 1-23 | 1-25 | 1-22 | | 1-24 |
| TM (1) | 24-46 | 26-48 | 23-45 | | 25-47 |
| inside | 47-58 | 49-60 | 46-65 | | 48-59 |
| TM (2) | 59-78 | 61-83 | 66-88 | | 60-82 |
| outside | 79-97 | 84-97 | 89-97 | | 83-96 |
| TM (3) | 98-120 | 98-120 | 98-120 | | 97-119 |
| inside | 121-140 | 121-139 | 121-140 | | 120-139 |
| TM (4) | 141-163 | 140-162 | 141-163 | | 140-162 |
| outside | 164-198 | 163-202 | 164-203 | | 163-201 |
| TM (5) | 199-221 | 203-25 | 204-226 | | 202-224 |
| inside | 222-240 | 226-237 | 227-237 | | 225-236 |
| TM (6) | 241-260 | 238-260 | 238-260 | | 237-259 |
| outside | 261-274 | 261-269 | 261-272 | | 260-268 |
| TM (7) | 75-292 | 270-289 | 273-292 | | 269-291 |
| inside | 293-314 | 290-318 | 293-323 | | 292-311 |

TABLE 13

| GENBANK IDENTIFIER | MOUSE HOMOLOG | 061779 | 061780 | 061781 | 061784 | 061785 |
|---------------------------|-------------------------------------|---------------|---------------|---------------|---------------|---------------|
| XM_061779 | | | 42% (63%) | 36% (57%) | 43% (64%) | 40% (61%) |
| XM_061780 | MOR239-6 (AY073489) 90% (93%) | | | 41% (60%) | 44% (62%) | 46% (67%) |
| XM_061781 | | 36% (57%) | 41% (60%) | | 43% (63%) | 40% (61%) |

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| | | | | | |
|-----------|-----------------|-----------|-----------|-----------|-----------|
| XM_061784 | MOR223 ~>85% | 43% (64%) | 44% (62%) | 43% (63%) | 81% (87%) |
| XM_061785 | MOR223 ~>85% | 40% (61%) | 46% (67%) | 40% (61%) | 81% (87%) |

TABLE 14

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| Gene ID (GeneID) | ACCN | Protein ID Expression Site | Other expression sites | Cytoplasmic domain |
|---------------------------------|-----------|----------------------------------|---|--------------------|
| TMD1030 (SEQ ID NO 185- 186) | XM_166853 | spleen | liver | 11q12.2 |
| TMD1029 (SEQ ID NO 187- 188) | XM_166854 | spleen, lymphocytes, liver | brain, heart, lung, lymph node | 11q12.2 |
| TMD1028 (SEQ ID NO 189- 190) | XM_166855 | spleen, lymphocytes | liver | 11q12.2 |
| TMD0621 (SEQ ID NO 191- 192) | XM_166205 | spleen | brain, heart, liver, lung and pancreas | 11q12.2 |

TABLE 15

| Gene ID | ACCN | Protein ID (GeneID) | Cytoplasmic domain |
|---------|-----------|------------------------|--|
| TMD1030 | XM_166853 | 298 | Transmembrane domain: 27 - 49 Transmembrane domain: 98 - 120 Transmembrane domain: 140 - 162 Transmembrane domain: 175 - 197 Transmembrane domain: 207 - 226 |

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| | | | |
|---------|-----------|-----|--|
| TMD1029 | XM_16684 | 309 | Transmembrane domain: 238 - 260 Transmembrane domain: 275 - 292 Transmembrane domain: 26 - 48 Transmembrane domain: 61 - 78 Transmembrane domain: 98 - 120 Transmembrane domain: 140 - 162 Transmembrane domain: 196 - 218 Transmembrane domain: 238 - 260 Transmembrane domain: 275 - 292 |
| TMD1028 | XM_166855 | 173 | Transmembrane domain: 18 - 40 Transmembrane domain: 61 - 83 Transmembrane domain: 103 - 125 Transmembrane domain: 137 - 156 |
| TMD0621 | XM_166205 | 109 | Transmembrane domain: 9-31 Transmembrane domain: 69 - 91 |

TABLE 17

| GeneID | ACCN | 5'-3' seq | 3'-5' seq | RefSeq |
|---------|-----------|--|-----------|--|
| TMD1030 | XM_166853 | GGGATTGTGGTCCAAACGAATTCA (SEQ ID NO 197) | | GAGCCTATATATATGAGCCAGCTACGACTTGA (SEQ ID NO 198) |
| TMD1029 | XM_166854 | GTCACACTGATTCTATTTCTGGGATTGGGC (SEQ ID NO 199) | | AAACCTGTTGTCAGGGCATTTTGAGGCC (SEQ ID NO 200) |
| TMD1028 | XM_166855 | GATATCATTTGGGGTGTATGATAAACATTATGG (SEQ ID NO 201) | | CTCCAACCCAGTGAATCATCAGTTAACATCCAC (SEQ ID NO 202) |
| TMD0621 | XM_166205 | TTAAGCTTATTAGTTAGTTCAATATCATGGGTTCC (SEQ ID NO 203) | | CTCTATTAAATACGATGGCATAGATAACATGTAAGAG (SEQ ID NO 204) |

TABLE 18

| GeneID | ACCN | 5'-3' seq (RefSeq) | 3'-5' seq (RefSeq) | RefSeq |
|---------|-----------|--|--|--------|
| TMD1030 | XM_166853 | ATGTTCCATCTAAATGAGCCTGAGAACCGAACACTACCCACTTGTAG ACATCCATTATAAACGGGTTAATATACCTGTAAGATAAGCCTAGA | (0.94) (SEQ ID NO 205) (0.95) (SEQ ID NO 206) | |
| TMD1029 | XM_166854 | AAATGTATTAATTCTGGATGAAATTGGGGTGGCTTGACTCTTTG | (0.98) (SEQ ID NO 207) | |
| TMD1028 | XM_166855 | ATGTTCCATCTAAATGAGCCTGAGAACCGAACACTACCCACTTGTAG ACATCCATTATAAACGGGTTAATATACCTGTAAGATAAGCCTAGA | (0.94) (SEQ ID NO 208) (0.95) (SEQ ID NO 209) | |

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| | | |
|----------|-----------|---|
| TMDB0621 | XN_166205 | AAATATATTTTAAATTGGCCAGGGGGTGGCTAACGCCTAATATCCC GGCTCAACGCCATAATCCAGACTTGGAGGCGAGGAGGTGGATCA TCCCAATATATATAACACACACACACACATATATTTAATCATTTAACAA CACACACATATATACACACACACATATACACACACATATACACAC (SEQ ID NO 210) (0.99) (SEQ ID NO 211) (0.97) (SEQ ID NO 212) (1.00) (SEQ ID NO 213) (0.91) (SEQ ID NO 213) |
|----------|-----------|---|

TABLE 19

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TABLE 19*(from Principles of Internal Medicine, Volume 1, Page 357, 12th Edition, McGraw-Hill Inc.)*

Table 20

| Gene ID | ACCN | Gene Name/Description | Predicted in Silico Expression | Observed expression |
|---------|-----------|---|--------------------------------|--|
| TMD077 | XM_166914 | Homo sapiens olfactory receptor MOR212-1 (LOC213956), mRNA. | pancreas and testis | brain, heart and kidney |
| TMD0233 | XM_069616 | Homo sapiens similar to olfactory receptor (LOC135941) mRNA | pancreas | none |
| TMD0256 | XM_066725 | Homo sapiens similar to olfactory receptor (LOC139478) mRNA | pancreas | skin and testis |
| TMD0258 | XM_066873 | Homo sapiens similar to beta-2 adrenergic receptor (LOC139760) mRNA | pancreas | colon, stomach and testis |
| TMD0267 | XM_089550 | Homo sapiens similar to CG5281 gene product (LOC159371) mRNA | pancreas and testis | adrenal gland, bone marrow, colon, heart, intestine(small), kidney, liver, pituitary, prostate, skin, stomach and thyroid |
| TMD0271 | XM_061815 | Homo sapiens similar to odorant receptor S18 gene (LOC120010) mRNA | pancreas and testis | PBL, prostate, thymus and uterus |
| TMD0290 | XM_065813 | Homo sapiens similar to unnamed protein product (LOC30644) mRNA | pancreas and testis | none |
| TMD0530 | XM_048304 | Homo sapiens hypothetical protein DKF2p56/A1164 (DKF2p56/A1164) mRNA | pancreas | brain, kidney, lung, lymph node, PBL, mammary gland, pituitary, stomach, testis and thyroid |
| TMD0574 | XM_055514 | Homo sapiens KIAA1910 protein (KIAA1910) mRNA | brain and pancreas | pituitary |
| TMD0608 | XM_058332 | Homo sapiens similar to putative (H. sapiens) (LOC118670) mRNA | pancreas and testis | stomach |
| TMD0639 | XM_058690 | Homo sapiens similar to data source:MGD; source key:MG:96073, evidence:ISS-hexosaminidase A-putative (LOC204249), mRNA. | pancreas and testis | liver, PBL and prostate |
| TMD0645 | XM_085376 | Homo sapiens LOC146225 (LOC146225), mRNA. | pancreas and testis | bone marrow, brain, heart, kidney, liver, lung, lymph node, PBL, muscle, pituitary, prostate, skin, spleen, stomach and thymus |
| TMD0674 | XM_059132 | Homo sapiens similar to RIKEN cDNA 4930549C01 gene (LOC127309) mRNA | pancreas and testis | brain, pituitary, prostate and stomach |
| TMD0675 | XM_059134 | Homo sapiens similar to putative (H. sapiens) (LOC127348) mRNA | pancreas and testis | prostate and stomach |
| TMD0677 | XM_059140 | Homo sapiens similar to dj39G22.2 (novel protein) (H. sapiens) (LOC127391) mRNA | pancreas and testis | prostate and stomach |
| TMD0726 | XM_059659 | Homo sapiens similar to hypothetical protein (H. sapiens) (LOC133309) mRNA | pancreas and testis | adrenal gland, brain, prostate and stomach |
| TMD0727 | XM_059654 | Homo sapiens similar to testis-specific transporter TST1 (H. sapiens) (LOC133482) mRNA | pancreas and testis | stomach |
| TMD0739 | XM_059812 | Homo sapiens similar to putative (H. sapiens) (LOC135886) mRNA | pancreas and testis | liver, lung, mammary gland, ovary, pituitary, prostate and stomach |
| TMD0753 | XM_059954 | Homo sapiens similar to putative (H. sapiens) (LOC138220) mRNA | pancreas and testis | none |
| TMD1111 | NM_014386 | Homo sapiens polycystic kidney disease 2-like 2 (PKD2L2) mRNA | pancreas and testis | none |
| TMD1127 | NM_054020 | Homo sapiens putative ion channel protein CATSPER2 (CATSPER2), mRNA. | pancreas and testis | none |

Table 21

| Clone ID | ACCN | Protein seq length (aa) | Domain description |
|----------|-----------|-------------------------|--|
| TMD0077 | XM_166914 | 310 | 7 transmembrane receptor (rhodopsin family) Transmembrane domains: 27 - 49 Transmembrane domains: 61 - 83 Transmembrane domains: 98 - 120 Transmembrane domains: 141 - 163 Transmembrane domains: 202 - 224 Transmembrane domains: 237 - 259 Transmembrane domains: 274 - 291 |
| TMD0233 | XM_069616 | 310 | 7 transmembrane receptor (rhodopsin family) Transmembrane domain: 26 - 48 Transmembrane domain: 60 - 77 Transmembrane domain: 97 - 119 Transmembrane domain: 140 - 162 Transmembrane domain: 196 - 218 Transmembrane domain: 239 - 261 Transmembrane domain: 272 - 291 |
| TMD0256 | XM_066725 | 308 | 7 transmembrane receptor (rhodopsin family) Transmembrane domain: 27 - 49 Transmembrane domain: 61 - 83 Transmembrane domain: 98 - 120 Transmembrane domain: 140 - 162 Transmembrane domain: 196 - 218 Transmembrane domain: 239 - 258 Transmembrane domain: 273 - 291 |
| TMD0258 | XM_066873 | 335 | 7 transmembrane receptor (rhodopsin family) Transmembrane domain: 10 - 32 Transmembrane domain: 39 - 61 Transmembrane domain: 79 - 101 Transmembrane domain: 121 - 143 Transmembrane domain: 163 - 185 Transmembrane domain: 226 - 248 Transmembrane domain: 263 - 282 |
| TMD0267 | XM_089550 | 324 | Integral membrane protein DUF6: 49-161 Transmembrane domain: 59 - 78 Transmembrane domain: 91 - 110 Transmembrane domain: 115 - 137 Transmembrane domain: 146 - 168 Transmembrane domain: 183 - 201 Transmembrane domain: 214 - 236 Transmembrane domain: 246 - 265 |

| | | | |
|---------|----------------------|-----|--|
| | | | Transmembrane domain: 270 - 292 |
| | | | Transmembrane domain: 297 - 316 |
| TMD0271 | XM_061815 | 291 | 7 transmembrane receptor (rhodopsin family) |
| | | | Transmembrane domain: 29 - 51 |
| | | | Transmembrane domain: 56 - 78 |
| | | | Transmembrane domain: 83 - 105 |
| | | | Transmembrane domain: 120 - 142 |
| | | | Transmembrane domain: 163 - 185 |
| | | | Transmembrane domain: 190 - 207 |
| | | | Transmembrane domain: 220 - 239 |
| | | | Transmembrane domain: 249 - 271 |
| TMD0290 | XM_065813 | 245 | Transmembrane domain: 24 - 46 |
| | | | Transmembrane domain: 61 - 83 |
| | | | Transmembrane domain: 96 - 118 |
| | | | Transmembrane domain: 128 - 150 |
| | | | Transmembrane domain: 162 - 184 |
| | | | Transmembrane domain: 221 - 243 |
| TMD0530 | XM_048304 | 708 | Immunoglobulin domain: 139-206 |
| | | | Immunoglobulin domain: 326-377 |
| | | | Transmembrane domain: 511 - 533 |
| TMD0574 | XM_055514 | 696 | Leucine rich repeat C-terminal domain: 212-262 |
| | | | Leucine rich repeat C-terminal domain: 529-579 |
| | | | Transmembrane domain: 621 - 643 |
| TMD0608 | XM_058332 | 105 | Transmembrane domain: 13 - 35 |
| TMD0639 | XM_058690 | 127 | Transmembrane domain: 12 - 34 |
| | | | Transmembrane domain: 44 - 66 |
| TMD0645 | XM_085376 | 248 | Transmembrane domain: 113 - 135 |
| | | | Transmembrane domain: 150 - 169 |
| | | | Transmembrane domain: 176 - 198 |
| TMD0674 | XM_059132 | 134 | Transmembrane domain: 5 - 22 |
| TMD0675 | XM_059134 | 206 | Transmembrane domain: 15 - 37 |
| TMD0677 | XM_059140 | 182 | Transmembrane: 49 - 71 |
| TMD0726 | XM_059639 | 96 | Transmembrane domain: 13 - 35 |
| | | | Transmembrane domain: 50 - 72 |
| TMD0727 | related to XM_059654 | 719 | Transmembrane domain: 108 - 130 |

| | | | |
|---------|-----------|-----|--|
| | | | Transmembrane domain: 145 - 164 |
| | | | Transmembrane domain: 171 - 193 |
| | | | Transmembrane domain: 229 - 251 |
| | | | Transmembrane domain: 264 - 286 |
| | | | Transmembrane domain: 314 - 336 |
| | | | Transmembrane domain: 421 - 443 |
| | | | Transmembrane domain: 453 - 475 |
| | | | Transmembrane domain: 580 - 602 |
| | | | Transmembrane domain: 668 - 690 |
| | | | Organic Anion Transporter Polypeptide (OATP) family, C-terminus: 125-473 |
| | | | Organic Anion Transporter Polypeptide (OATP) family, N-terminus: 558-717 |
| TMD0739 | XM_059812 | 265 | Transmembrane domain: 126 - 148 |
| | | | Transmembrane domain: 185 - 207 |
| TMD0753 | XM_059954 | 161 | Transmembrane domain: 26 - 48 |
| TMD1111 | NM_014386 | 609 | Ion transporter domain: 284-490 |
| | | | Transmembrane domain: 34 - 56 |
| | | | Transmembrane domain: 274 - 296 |
| | | | Transmembrane domain: 315 - 337 |
| | | | Transmembrane domain: 364 - 386 |
| | | | Transmembrane domain: 407 - 429 |
| | | | Transmembrane domain: 469 - 491 |
| TMD1127 | NM_054020 | 528 | Ion transporter domain: 172-340 |
| | | | Transmembrane domain: 113 - 132 |
| | | | Transmembrane domain: 147 - 169 |
| | | | Transmembrane domain: 176 - 198 |
| | | | Transmembrane domain: 241 - 263 |
| | | | Transmembrane domain: 276 - 295 |
| | | | Transmembrane domain: 315 - 337 |

Table 22

| Clone ID | ACCN | Cytogenetic locus | Disease linkage |
|----------|----------------------|-------------------|--|
| TMD0077 | XM_166914 | 11q12.2 | angioedema, hereditary; spastic paraplegia 17; osteoporosis-pseudoglioma syndrome; pancreatic tumor |
| TMD0233 | XM_069616 | 7q35 | glaucoma 1, open angle, f; |
| TMD0256 | XM_066725 | Xq26.1 | x inactivation, familial skewed, 2; panhypopituitarism; thoracoabdominal syndrome; dandy-walker malformation with mental retardation, basal ganglia disease, and seizures; split-hand/foot malformation 2; mental retardation with optic atrophy, deafness |
| TMD0258 | XM_066873 | Xq26.1 | x inactivation, familial skewed, 2; panhypopituitarism; thoracoabdominal syndrome; dandy-walker malformation with mental retardation, basal ganglia disease, and seizures; split-hand/foot malformation 2; mental retardation with optic atrophy, deafness |
| TMD0267 | XM_089550 | 10q24.1 | corneal dystrophy of bowman layer, type ii; alzheimer disease 6 |
| TMD0271 | XM_061815 | 11p15.4 | charcot-marie-tooth disease, type 4b, form 2; deafness, neurosensory, autosomal recessive 18; |
| TMD0290 | XM_065813 | 2p23.1 | none |
| TMD0530 | XM_048304 | 19q13.13 | hypocalciuric hypercalcemia, familial, type iii; deafness, autosomal dominant nonsyndromic sensorineural 4; microcephaly; primary autosomal recessive, 2 |
| TMD0574 | XM_055514 | 13q31.1 | microcoria, congenital; schizophrenia 7; |
| TMD0608 | XM_058332 | 10q26.3 | endometrial carcinoma |
| TMD0639 | XM_058690 | 15q22.32 | cataract, central saccular, with sutural opacities; obesity syndrome |
| TMD0645 | XM_085376 | 16q23.1 | dehydrated hereditary stomatocytosis; pancreatic acinar cancer |
| TMD0674 | XM_059132 | 1p36.11 | breast cancer, ductal, 2; prostate cancer/brain cancer susceptibility; melanoma, cutaneous malignant; inflammatory bowel disease 7; |
| TMD0675 | XM_059134 | 1p33 | carcinoma of pancreas |
| TMD0677 | XM_059140 | 1p34.2 | deafness, autosomal dominant nonsyndromic sensorineural 2; porphyria cutanea tarda; hypercholesterolemia, familial, ptosis, hereditary congenital 1 |
| TMD0726 | XM_059639 | 10q11.22 | none |
| TMD0727 | related to XM_059654 | 5q21.1 | anemia, dyserythropoietic congenital, type iii; dyslexia, specific, 1; colorectal cancer, hereditary nonpolyposis, type 7; cataract, central saccular, with sutural opacities |
| TMD0739 | XM_059812 | 7q11.23 | autism, susceptibility to, 1; muscular dystrophy, limb-girdle, type 1d; aneurysm, intracranial |
| TMD0753 | XM_059954 | 9q21.12 | hemophagocytic lymphohistiocytosis, familial, 1; amyotrophic lateral sclerosis with frontotemporal dementia |
| TMD1111 | NM_014386 | 5q31 | none |
| TMD1127 | NM_054020 | 15q13-q15 | nanophthalmos 2; spastic paraplegia 11, autosomal recessive; corpus callosum, agenesis of, with neuropathy, pancreatic acinar carcinoma |

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TABLE 23

| CODE | ACCN | PRIMERS | PROMOTER |
|------------------------------------|--|---|--|
| TMD0077 (SEQ ID NO 214- 215) | XM_166914 (SEQ ID NO 256) CACCAAGAATCACCACCATGGAAGCA (Reverse) (SEQ ID NO 257) | TCATGGTACCCAGTCACGGCTC (Forward) (SEQ ID NO 255) TGCTGACGATCTTATGAAACAGG (Forward) (SEQ ID NO 259) TCACGTCAGGCTCTCCTCAGTG (Reverse) (SEQ ID NO 260) | GGATTCAAGGCCCTTTAAACCCCCACTAGGGGCGATGGCAGGGCTTTGA (0.88) (SEQ ID NO 258) |
| TMD0233 (SEQ ID NO 216- 217) | XM_069616 (SEQ ID NO 261) | TCACAAATCATATAATTAGGGAAAAGAGAGAGGGCAGGTATACTCTAAAAA (SEQ ID NO 261) AATTTCCTTAATGACCTCAGAAATGTCACCATGCTTAGTTATTTTA (0.95) (SEQ ID NO 262) | TCACAAATCATATAATTAGGGAAAAGAGAGAGGGCAGGTATACTCTAAAAA (SEQ ID NO 259) AATTTCCTTAATGACCTCAGAAATGTCACCATGCTTAGTTATTTTA (0.95) |
| TMD0236 (SEQ ID NO 218- 219) | XM_066725 (SEQ ID NO 263) AGCAGACACAATACTGGCCATTCAAACAC (Reverse) (SEQ ID NO 264) | GGCCATGGACAATGTACAGCAG (Forward) (SEQ ID NO 263) GGTACTATTCCTATTTGGGACACAGCAAATGAAAGAAAACAGAAAACC (0.93) (SEQ ID NO 265) CTGGGTTCATAAATATGGAGCAGAAAGTTTACAAATTAGAACAGCA (0.92) (SEQ ID NO 266) TAGAAATGTTTATAAAAAATGAAACAGGGCTAGGGAAAGAGATGGTGA (0.91) (SEQ ID NO 267) | CCAAGGAACATTAAACCTCCATTGCACAGTTACCCCCAGAATATTAA (0.97) (SEQ ID NO 270) CATCCTGGAAATAATTGGCGTCCAACTCTGCACCTTGCTCTCTATTCCCT (0.96) (SEQ ID NO 271) CTGGGGCCCTCAAAAAGCTCACCTCCCTCACTTCCCACCTCAACTGT (0.91) (SEQ ID NO 272) |
| TMD0238 (SEQ ID NO 220- 221) | XM_066873 (SEQ ID NO 268) | CCTCAATTGGCTTCCCACTCG (Forward) (SEQ ID NO 268) GCCATCAAACTCTGAGCTGGAGATA GTGAC (Reverse) (SEQ ID NO 269) | AAACGGCATTTTAAAATGCAAGTTTAAATTGTTATCCCATCTATGGTT (0.98) (SEQ ID NO 275) |
| TMD0267 (SEQ ID NO 222- 223) | XM_089550 (SEQ ID NO 273) | TGGCCTCGTTGAAAGTGTCA TCA TCC (Forward) TTGGTACCATTTACGAATGGCCGC (Reverse) (SEQ ID NO 274) | ATTTGGTTATATAGAGGAGCTAGGAAAGACTCTGGGCTCTGATTC (0.97) (SEQ ID NO 278) TACTCATTTATATAGCAGCAA CCTTACATGGCCAGGAGAACTCACT (0.94) (SEQ ID NO 279) |
| TMD0271 (SEQ ID NO 224- 225) | XM_061815 (SEQ ID NO 276) | CTGGACTTGGCA GTTACCA CGTCTGGATC (Forward) (SEQ ID NO 276) CATATTCCACACCCAATT TGACA ATGG (Reverse) (SEQ ID NO 277) | CTGAAATTACATAAAAGGACTTGGAGGCTTGCAGCAACTTGCAT (0.97) (SEQ ID NO 282) TTTCCTCTTTAAAACACGCTTCACTCTCAAAACAGCAGAGAAATGAA (0.98) (SEQ ID NO 283) AACTGGGTCTATAAGAGGCCAGGGCACTTATTCACTCCAGGGCAAGATG (0.99) (SEQ ID NO 284) |
| TMD0290 (SEQ ID NO 226- 227) | XM_065813 (SEQ ID NO 281) | GTTACCCACCCACCGTACGACC (Forward) (SEQ ID NO 280) CAGGGCATGCCAGAGAACGATG (Reverse) | GGCGAGGATAAGGGAGTCCAA TCCACGGGCCCCAGTATGGTGA (0.86) (SEQ ID NO 287) |
| TMD0530 (SEQ ID NO 228- 229) | XM_048304 (SEQ ID NO 285) | CTATGACTTCACACCTGGCA (Forward) AAGGTGGCCA ACTTGTCTGGCTC (Reverse) (SEQ ID NO 286) | |

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| CODE | ACCN | PRIMERS | PROMOTER |
|------------------------------------|-----------|---|---|
| TMD0574 (SEQ ID NO 230. 231) | XM_055514 | TCAATGCCATTGCCCAAACCTGAGGA (Forward) (SEQ ID NO 288) CAACACCGAGATGGACCCCTGCT (Reverse) (SEQ ID NO 289) | CTTTAAGTTAAAAATGTGGGTTTAGATGATTGTCCTTCTAAACAGC (0.99) (SEQ ID NO 290) TCAGGATGTCATAAAAAGATCTCTAGTGTACACACGTGCACACACA (0.97) (SEQ ID NO 291) AGTAACCTTATTAAAAGACCTAAATTCCTAAATGATCTAT (0.90) (SEQ ID NO 292) AATAAATTTAAAAGACTCCTTCCGAATGGGAGCTGGTGGGGC (0.91) (SEQ ID NO 293) |
| TMD0608 (SEQ ID NO 232- 233) | XM_058332 | CTCAGGACGAAGATCATGATCGGCATC (Forward) (SEQ ID NO 294) GAAGATTTTGTGCCCAAGCTTCCCAAAG (Reverse) (SEQ ID NO 295) | TATTCCTACTTAACTGGGAGCTAACCCATGAGGGACCAAGGCATAAG (0.99) (SEQ ID NO 296) TTACATATGTTACATGTGCCATGCTGGTGTGCTGACCCATTAACCTCGT (0.96) (SEQ ID NO 297) |
| TMD0639 (SEQ ID NO 234- 235) | XM_058690 | TCCATGCTCAGCTTCATTCAGCTAC (Forward) (SEQ ID NO 298) TCCATCTCAAGACCTTGCCCCCTTCA (Reverse) (SEQ ID NO 299) | AATAAACCCATTAAAAAGTGGGAAAGGCATGAACACCTTCAAAAGA (1.00) (SEQ ID NO 300) |
| TMD0645 (SEQ ID NO 236- 237) | XM_085376 | AGGACGGTAAAGGAGCCATGGGACA (Forward) (SEQ ID NO 301) CTTGGCCAGGTTCTGGTGGCTGG (Reverse) (SEQ ID NO 302) | TCTTTTGTCTATAAATAGGACTTTGATTTCTGGACTAGAGAAATTGTAT (0.94) (SEQ ID NO 303) |
| TMD0674 (SEQ ID NO 238- 239) | XM_059132 | ACGACTCCAAAGAACAGGAAGGCCG (Forward) (SEQ ID NO 304) AAGGTAAACATCGGCAAGGCCAGC (Reverse) (SEQ ID NO 305) | GCTAGGCAATTTTAAAGCTGATGTCCTCACTGGGACGGGACTTCACAC (0.94) (SEQ ID NO 306) |
| TMD0675 (SEQ ID NO 240- 241) | XM_059134 | CGGGCAAGTACCAAAAGCTCAGCTG (Forward) (SEQ ID NO 307) GCCAGATTCAAGGAGAATGGAAGAAC (Reverse) (SEQ ID NO 308) | TGATCTACTTTAAAGGATCATGGCTGCTGGGATTAGGATA (0.91) (SEQ ID NO 309) TGATAGTGTATAAAAAAGTGGCCAGATTGGTTTATTTGAAATAAA (0.99) (SEQ ID NO 310) TATAGTGTATAATTAAAGCCAGGGCTGGTGAAGATAACTGATGGAAATGA (0.93) (SEQ ID NO 311) ATGGGAGGACTATAAAAGAGGGAGTCATTAAAATGGTGTCAAGAAGGCTGA (0.96) (SEQ ID NO 312) AGAGGGGAGGTCAATTAAAATGGTGTAAAGAAGCTGAGCTACAGCAGTGGT (0.97) (SEQ ID NO 313) GACATTCCACCCAAAAATGCCACTGGATGAAGTCCCCCTCTCCATTAA (0.92) (SEQ ID NO 314) |

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| CODE | ACCN | PRIMERS | PROMOTER |
|------------------------------------|---|---|---|
| TMD0677 (SEQ ID NO 242- 243) | XM_059140 | TTGGGAGAGACTGTGACCTCAGCA (Forward) (SEQ ID NO 315) GAGCAATCCCTCTTCGTCAGGT (Reverse) (SEQ ID NO 316) | AAAAAGTGCCTTTAAACAGGGGGTGGAGGGCTTATGAGAAAGGGACCA (1.00) (SEQ ID NO 317) CCATTCTACTAAAATGCAGAGATCAGCCAGCGTGGCACGTGCCTGTA (0.95) (SEQ ID NO 318) AAAAAAAGGGCTGTTTATATCTTACCTCCCTGGCTGGGTGC (0.98) (SEQ ID NO 319) AAAAATAAAAATAAAAAAATCCCCATTCAACCTCAAT (0.93) (SEQ ID NO 320) |
| TMD0726 (SEQ ID NO 244- 245) | XM_059639 | ACTTCCCACATCTACAACCTCCTCAGAGTCATT (Forward) (SEQ ID NO 321) TGCAAGCACCATCTGTAAGGACAA (Reverse) (SEQ ID NO 322) | TTTTTTAAACTATAAAAAGTGGGATCAGAAAACAGTCATAAGGGAAA (0.97) (SEQ ID NO 323) GTATATGCTATAATATCAGGATTCACTTAAATGGCATTGAGTTCAGGA (0.98) (SEQ ID NO 324) ATAAACAAATTTAAAATTAGGCCACCATGGTTGACACACCTGTGTTCT (0.99) (SEQ ID NO 325) AAAAAAGTGAAGGGGGAGACTTTAACCTCTGAAATATATT (0.92) (SEQ ID NO 326) |
| TMD0727 (SEQ ID NO 246- 247) | XM_059634 (related to) TGACAGAGCTAGGCATATGAGCACTCGA (Reverse) | CCAAGAAGCCGGGAGAAGTGGATG (Forward) (SEQ ID NO 327) (SEQ ID NO 328) | CTAAAGAGCTTATATTCAGGCTAAAGAAAACCAATAAGAAAGTGC (0.96) (SEQ ID NO 329) |
| TMD0739 (SEQ ID NO 248- 249) | XM_059812 | GGAGTTGGTTCAAGAACCGAGATCAC (Forward) (SEQ ID NO 330) GGCAGATGGGATACATTCTCTGGG (Reverse) (SEQ ID NO 331) | ACTAAAAAAATACAAAAAAAGTAGCCGGTATGGTGGTAGGGCTTATAATCC (0.93) (SEQ ID NO 332) GGTAGGGCGCTATAATCCCAAGCTACTTGGGGTGGCAGGAGAAATTG (0.92) (SEQ ID NO 333) |
| TMD0733 (SEQ ID NO 250- 251) | XM_059954 | TGGGCTTGGAAAATCAGAAATGAGAAGG (Forward) (SEQ ID NO 334) TGCAACAAAGGAATGATTGCAAGCAGTAG (Reverse) (SEQ ID NO 335) | AAAAAGGCTTATAAAAGGTTTGTGTTGGAGACGGAGTT (0.97) (SEQ ID NO 336) GGGCCAACCTTATAAAAGGTTATGTTTTGTTCTGATAATTTCGTTTCT (0.91) (SEQ ID NO 337) AAAGTTAAGTTTAAAAGAACAGGCTACAAAGTTATAGCTTATGGGTGAT (0.96) (SEQ ID NO 338) |
| TMD1111 (SEQ ID NO 252- 253) | NM_014386 | GGGGCGGTGTTAGTGCAGGTCGG (Forward) (SEQ ID NO 339) CCTCCAGTGCAGGGAAATTCTGCC (Reverse) | AATTCAAATTTTAAACGGACTGTCTCCTCTTCAAAAAGTCTAGATCT (0.92) (SEQ ID NO 341) |
| TMD1127 (SEQ ID NO 254- 255) | NM_034020 | GGCTGTGTTGAGCAGGGCTTCATGTGC (Forward) (SEQ ID NO 342) CTCCCTCTGAGATGATCTGCCGCTTG (Reverse) (SEQ ID NO 343) | ATGGGGTGCATATATTTAGGATAGTTAGCTCTCTGTGAATTGATC (0.89) (SEQ ID NO 344) |

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CLAIMS:

1. A method of detecting an immune system cell, comprising:

contacting a sample comprising cells with a polynucleotide specific for TMD0024

(XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025

5 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304

(XM_060956), TMD0888 (XM_060957), or TMD0890 (XM_060959) of claim 28, under conditions effective for said polynucleotide to hybridize specifically to said gene, and

detecting specific hybridization.

10 2. A method of claim 1, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

15 3. A method of detecting an immune system cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for by TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), or TMD0890 (XM_060959) of claim 28, under conditions effective for said binding partner bind specifically to said polypeptide, and

20 detecting specific binding.

25 4. A method of claim 3, wherein said detecting is performed by:

immunocytochemistry, immunoprecipitation, or Western blot.

5. A method of delivering an agent to an immune cell, comprising:

contacting an immune cell with an agent coupled to binding partner specific for a polypeptide coded for by TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), or TMD0890 (XM_060959) of claim 28 , whereby said agent is delivered to said cell.

6. A method of claim 5, wherein the agent is a therapeutic agent or an imaging agent.

7. A method of claim 5, wherein the agent is cytotoxic.

8. A method of claim 5, wherein the binding partner is an antibody.

5

9. A method of modulating the maturation of an immune system cell, comprising:

contacting said cell with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28, whereby the maturation of an immune cell is modulated.

10

10. A method of modulating interactions between lymphoid and non-lymphoid immune system cells, comprising:

15 contacting said cells with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28, whereby the interaction is modulated.

20

11. A method of expressing a heterologous polynucleotide in immune system cells, comprising:

expressing a nucleic acid construct in immune system cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said 25 promoter sequence is selected from SEQ ID NOS 5, 10, 11, 16-19, 29-32, 37-39, 44-46, 51-54, and 59-62.

12. A method of treating an immune system disease, comprising:

30 administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of a gene, or polypeptide encoded thereby, selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025

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(XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304
(XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28.

13. A method of claim 12, wherein said agent is an antibody or an antisense which is

5 effective to inhibit translation of said gene.

14. A method of diagnosing an immune disease associated with abnormal gene expression,
or determining a subject's susceptibility to such disease, comprising:

assessing the expression of a gene, or polypeptide encoded thereby, selected from

10 TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025
(XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304
(XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28 in a
tissue sample comprising immune system cells.

15 15. A method of claim 14, wherein assessing is:

measuring expression levels of said gene, determining the genomic structure of said
gene, determining the mRNA structure of transcripts from said gene, or measuring the
expression levels of polypeptide coded for by said gene.

20 16. A method of claim 14, wherein said assessing detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,
RACE PCR, or *in situ* hybridization, and

using a polynucleotide probe having a sequence selected from TMD0024
(XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025
25 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304
(XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28, or a
polynucleotide probe having 95% sequence identity or more to a sequence set forth in SEQ
ID NOS 1, 6, 12, 20, 25, 33, 40, 47, or 55, effective specific fragments thereof, or
complements thereto.

30

17. A method of assessing a therapeutic or preventative intervention in a subject having an

immune system disease, comprising,

determining the expression levels of a gene, or polypeptide encoded thereby, selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28 in a tissue sample comprising immune system cells.

18. A method of claim 17, further comprising assessing the expression levels of a plurality of said genes or polypeptides.

10

19. A method for identifying an agent that modulates the expression of a gene or polypeptide in the immune system gene complex, comprising,

contacting an immune system cell with a test agent under conditions effective for said test agent to modulate the expression of a gene selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28, or the biological activity of a polypeptide encoded thereby, in said immune system cell, and

determining whether said test agent modulates said gene or polypeptide.

20

20. A method of claim 19, wherein said agent is an antisense polynucleotide which is effective to inhibit translation of said gene or an antibody specific for said polypeptide.

25 21. A method of detecting polymorphisms in a gene in the immune system gene complex, comprising: comparing the structure of:

genomic DNA or RNA or cDNA or a polypeptide comprising all or part of a gene selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28 with the structure of SEQ ID NOS 1, 6, 12, 20, 25, 33, 40, 47, or 55.

22. A method of claim 20, wherein said polymorphism is a nucleotide deletion, substitution, inversion, or transposition.

5 23. A method of identifying a genetic basis for an immune disease or disease-susceptibility, comprising:

determining the association of an immune disease or disease-susceptibility with a nucleotide sequence present in a genome comprising the gene complex of claim 28.

10 24. A method of claim 23, wherein determining is performed by producing a human-linkage map of said complex.

25. A method of claim 23, wherein determining is performed by comparing the nucleotide sequences between normal subjects and subjects having an immune system disease.

15 26. A non-human, transgenic mammal, or a cell thereof, whose genome comprises a functional disruption of a gene selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) of claim 28, or a mouse homolog thereof, and which has a defect in immune system function.

27. A method of selecting a gene predominantly expressed in immune system cells from a database comprising polynucleotide sequences for genes, comprising:

displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide sequence for a gene selected from TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890

5 (XM_060959), or complements to the polynucleotides sequence,

wherein said displayed sequences have been retrieved from said database upon selection by a user.

28. A composition consisting essentially of the 1q22 immune gene complex, comprising

10 TMD0024 (XM_060945), TMD1779 (XM_060946), TMD0884 (XM_060947), TMD0025 (XM_060948), TMD1780 (XM_089422), TMD1781 (XM_089421), TMD0304 (XM_060956), TMD0888 (XM_060957), and TMD0890 (XM_060959) genes, or a fragment thereof comprising at least two said genes.

15 29. A composition of claim 28, wherein said complex consists essentially of the chromosome region between STS markers SHGC-81033 and SHGC-145403, or a fragment thereof comprising at least two said genes.

20 30. A composition of claim 28, wherein said complex consists essentially of the chromosome region between STS markers SHGC-81033 and D1S3249, G15944, GDB:191077, or GDB:196442, or a fragment thereof comprising at least two said genes.

25 31. A composition of claim 28, wherein said complex consists essentially of the chromosome region between STS markers RH118729 and D1S2577 or SHGC-145403, or a fragment thereof comprising at least two said genes.

32. A method of detecting an immune system cell, comprising:
contacting a sample comprising cells with a polynucleotide specific for a XM_062147 (SEQ ID NO 63) or XM_061676 (SEQ ID NO 69) of claim 59 under conditions effective for
30 said polynucleotide to hybridize specifically to said gene, and
detecting specific hybridization.

33. A method of claim 32, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

5 34. A method of detecting an immune system cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for XM_062147 (SEQ ID NO 64) or XM_061676 (SEQ ID NO 70) of claim 59 under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding.

10

35. A method of claim 34, wherein said detecting is performed by:

immunocytochemistry, immunoprecipitation, or Western blot.

36. A method of delivering an agent to an immune cell, comprising:

15

contacting an immune cell with an agent coupled to binding partner specific for XM_062147 (SEQ ID NO 64) or XM_061676 (SEQ ID NO 70) of claim 59, whereby said agent is delivered to said cell.

37. A method of claim 36, wherein the agent is a therapeutic agent or an imaging agent.

20

38. A method of claim 36, wherein the agent is cytotoxic.

39. A method of claim 36, wherein the binding partner is an antibody.

25

40. A method of modulating the maturation of an immune system cell, comprising:

contacting said cell with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59, whereby the maturation of an immune cell is modulated.

30

41. A method of modulating interactions between lymphoid and non-lymphoid immune system cells, comprising:

contacting said cells with an agent effective to modulate a gene, or polypeptide encoded thereby, selected from XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59, whereby the interaction is modulated.

5 42. A method of expressing a heterologous polynucleotide in immune system cells, comprising:

expressing a nucleic acid construct in immune system cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is SEQ ID NOS 65, 66, 72, 73, 74, or 75.

10

43. A method of treating an immune system disease, comprising:

administering to a subject in need thereof a therapeutic agent which is effective for regulating expression of a gene, or polypeptide encoded thereby, selected from XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59.

15

44. A method of claim 43, wherein said agent is an antibody or an antisense which is effective to inhibit translation of said gene.

20 45. A method of diagnosing an immune disease associated with abnormal gene expression, or determining a subject's susceptibility to such disease, comprising:

assessing the expression of a gene, or polypeptide encoded thereby, selected from XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59 in a tissue sample comprising immune system cells.

25 46. A method of claim 45, wherein assessing is:

measuring expression levels of said gene; determining the genomic structure of said gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene.

30 47. A method of claim 45, wherein said assessing detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,

RACE PCR, or *in situ* hybridization, and
using a polynucleotide probe having a sequence selected from SEQ ID NOS 67, 68,
76, and 77.

5 48. A method of assessing a therapeutic or preventative intervention in a subject having an
immune system disease, comprising,

 determining the expression levels of a gene, or polypeptide encoded thereby, selected
from XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59
in a tissue sample comprising immune system cells.

10

49. A method of claim 48, further comprising assessing the expression levels of a plurality
of said genes or polypeptides.

15 50. A method for identifying an agent that modulates the expression of a gene or polypeptide
in the immune system gene complex, comprising,

 contacting an immune system cell with a test agent under conditions effective for said
test agent to modulate the expression of XM_062147 (SEQ ID NO 63 or 64) or XM_061676
(SEQ ID NO 69 or 70) of claim 59, or a polypeptide encoded thereby, in said immune system
cell, and

20

 determining whether said test agent modulates said gene.

51. A method of claim 50, wherein said agent is an antisense polynucleotide to a target
polynucleotide sequence selected from SEQ ID NOS 63 or 69 and which is effective to
inhibit translation of said gene.

25

52. A method of detecting polymorphisms in a gene in the immune system gene complex,
comprising:

 comparing the structure of: genomic DNA or RNA or cDNA comprising all or part
of an allele of XM_062147 or XM_061676 with SEQ ID NOS 63 or 69 of claim 59.

30

53. A method of claim 52, wherein said polymorphism is a nucleotide deletion, substitution,

inversion, or transposition.

54. A non-human, transgenic mammal whose genome comprises a functional disruption of a gene represented by XM_062147 (SEQ ID NO 63) or XM_061676 (SEQ ID NO 69) of claim 59, and which has a defect in immune system function.

55. A mammalian immune system cell whose genome comprises a functional disruption of a gene represented by XM_062147 (SEQ ID NO 63) or XM_061676 (SEQ ID NO 69) of claim 59, and which has a defect in immune system function.

10

56. A mammalian cell of claim 55, wherein said cell is a mouse cell.

57. A non-human, transgenic mammal, or a cell thereof, comprising a gene operatively linked to an expression control sequence effective to express said gene in immune system, 15 wherein said sequence is SEQ ID NOS 65, 66, 71, 72, 73, 74, or 75.

58. A method of selecting a gene predominantly expressed in immune system cells from a database comprising polynucleotide sequences for genes, comprising:

20 displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide sequence for XM_062147 (SEQ ID NO 63 or 64) or XM_061676 (SEQ ID NO 69 or 70) of claim 59, or complements to the polynucleotides sequence,

wherein said displayed sequences have been retrieved from said database upon selection by a user.

25 59. A composition comprising:

bone marrow specific genes consisting essentially of XM_062147 (SEQ ID NO 63 or 64) and XM_061676 (SEQ ID NO 69 or 70), or polypeptides thereof.

60. A method of detecting a kidney cell, comprising:

30 contacting a sample comprising cells with a polynucleotide specific for a polynucleotide, or a naturally-occurring polymorphisms thereof, of claim 81 under conditions effective for said polynucleotide to hybridize specifically to said gene, and

detecting specific hybridization.

61. A method of claim 60, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,

5 RACE PCR, or *in situ* hybridization.

62. A method of detecting an kidney cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for by a polynucleotide of claim 81, or a naturally-occurring polymorphism thereof,
10 under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding.

63. A method of claim 62, wherein said detecting is performed by: immunocytochemistry, immunoprecipitation, or Western blot.

15

64. A method of delivering an agent to a kidney cell, comprising:

contacting a kidney cell with an agent coupled to binding partner specific for polypeptide coded for by a polynucleotide of claim 81, or a naturally-occurring polymorphism thereof, whereby said agent is delivered to said cell.

20

65. A method of claim 64, wherein the agent is a therapeutic agent, a cytotoxic agent, or an imaging agent.

66. A method of claim 64, wherein the binding partner is an antibody.

25

67. A method of modulating a kidney cell, comprising:

contacting said cell with an agent effective to modulate a polynucleotide, or polypeptide encoded thereby, or a naturally-occurring polymorphism thereof, of claim 81, whereby the kidney cell is modulated.

30

68. A method of assessing kidney function, comprising:

detecting a polypeptide coded for by a polynucleotide of claim 81, or a naturally-occurring polymorphism thereof, or fragments thereof, in a body fluid, whereby the amount of said polypeptide in said fluid is a measure of kidney function.

5 69. A method of claim 68, wherein said detecting is performed using an antibody which is specific for said polypeptide.

70. A method of claim 69, wherein said detecting is performed by RIA, ELISA, or Western blot.

10

71. A method of expressing a heterologous polynucleotide in kidney cells, comprising:

expressing a nucleic acid construct in kidney cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected from SEQ ID NOS. 106, 109, 110, 113, 114, 117, 118, 121,

15 124, 125, 128-130, 133, 134, 137, 140, 141, 144, 147, 148, and 151.

72. A method of diagnosing a kidney disease associated with abnormal gene expression, or determining a subject's susceptibility to such disease, comprising:

assessing the expression of a polynucleotide of claim 81, or a polypeptide encoded

20 thereby, or naturally-occurring polymorphisms thereof, in a tissue sample comprising kidney cells.

73. A method of claim 72, wherein assessing is:

measuring expression levels of said gene, determining the genomic structure of said 25 gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene.

74. A method of assessing a therapeutic or preventative intervention in a subject having a kidney disease, comprising,

30 determining the expression levels of a polynucleotide of claim 81, a naturally-occurring polymorphism thereof, or polypeptide encoded thereby, in a tissue sample

comprising kidney cells.

75. A method of claim 74, further comprising assessing the expression levels of a plurality of said genes or polypeptides.

5

76. A method for identifying an agent that modulates the expression of a polynucleotide or polypeptide selectively expressed in kidney cells, comprising,

contacting an kidney cell with a test agent under conditions effective for said test agent to modulate the expression of a polynucleotide of claim 81, or a naturally-occurring polymorphism thereof, or the biological activity of a polypeptide encoded thereby, in said kidney cell, and

determining whether said test agent modulates said gene or polypeptide.

10 77. A non-human, transgenic mammal whose genome comprises a functional disruption of a gene represented by a polynucleotide of claim 81, or a homolog thereof, and which has a defect in kidney function.

15 78. A mammalian kidney cell whose genome comprises a functional disruption of a gene represented by a polynucleotide of claim 81, or a homolog thereof, and which has a defect in kidney function.

20 79. A mammalian cell of claim 78, wherein said cell is a mouse cell.

80. A method of selecting a gene predominantly expressed in kidney cells from a database
25 comprising polynucleotide sequences for genes, comprising:

displaying, in a computer-readable medium, a polynucleotide sequence, or a polypeptide encoded thereby, of claim 81, or complements to the polynucleotides sequence, wherein said displayed sequences have been retrieved from said database upon selection by a user.

5

81. A composition comprising two or more of the following polynucleotides expressed selectively in kidney:

TMD0049 (XM_057351), TMD0190 (XM_087157), TMD0242 (XM_088369),
TMD0335 (XM_089960), TMD0371, TMD0374, TMD0469 (XM_038736), TMD0719
10 (XM_059548), TMD0731 (XM_059703), TMD0785 (XM_060310), TMD0841
(XM_060623), TMD1114 (NM_019841), and/or TMD 1148 (XM_087108).

82. A method of detecting a pancreas cell, comprising:

contacting a sample comprising cells with a polynucleotide specific for TMD0986,
15 XM_061780, XM_061781, XM_061784, or XM_061785, of claim 113 under conditions effective for said polynucleotide to hybridize specifically to said gene, and detecting specific hybridization.

83. A method of claim 82, wherein said detecting is performed by:

20 Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

84. A method of detecting a pancreas cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for by TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, of claim 25 113 under conditions effective for said binding partner bind specifically to said polypeptide, and, detecting specific binding.

85. A method of claim 84, wherein said detecting is performed by:

immunocytochemistry, immunoprecipitation, or Western blot.

30

86. A method of delivering an agent to a pancreas cell, comprising:

contacting a pancreas cell with an agent coupled to binding partner specific for

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TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, of claim 113, whereby said agent is delivered to said cell.

87. A method of claim 86, wherein the agent is a therapeutic agent or an imaging agent.

5

88. A method of claim 86, wherein the agent is cytotoxic.

89. A method of claim 86, wherein the binding partner is an antibody.

10 90. A method of modulating a pancreas cell, comprising:

contacting said cell with an agent effective to modulate TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, or the biological activity of a polypeptide encoded thereby, of claim 113, whereby the pancreas cell is modulated.

15 91. A method of assessing pancreas function, comprising:

detecting a polypeptide coded for TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, or fragments thereof, in a body fluid, whereby the amount of said polypeptide in said fluid is a measure of pancreas function.

20 92. A method of claim 91, wherein said detecting is performed using an antibody which is specific for said polypeptide.

93. A method of claim 91, wherein said detecting is performed by RIA, ELISA, or Western blot.

25

94. A method of expressing a heterologous polynucleotide in pancreas cells, comprising:
expressing a nucleic acid construct in pancreas cells, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is SEQ ID NOS 156-161, 166, 179; or 180.

30

95. A method of diagnosing a pancreas disease associated with abnormal gene expression,

or determining a subject's susceptibility to such disease, comprising:

assessing the expression of TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, or polypeptide encoded thereby, of claim 113 in a tissue sample comprising pancreas cells.

5

96. A method of claim 95, wherein assessing is:

measuring expression levels of said gene, determining the genomic structure of said gene, determining the mRNA structure of transcripts from said gene, or measuring the expression levels of polypeptide coded for by said gene.

10

97. A method of claim 95, wherein said assessing is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization, and

using a polynucleotide probe having a sequence selected from SEQ ID NOS 154, 155, 15 164, 165, 169, 170, 173, 174, 177, 178, or a complement thereto.

98. A method of assessing a therapeutic or preventative intervention in a subject having a pancreas disease, comprising,

determining the expression levels of TMD0986, XM_061780, XM_061781, 20 XM_061784, or XM_061785, or a polypeptide encoded thereby, of claim 113 in a tissue sample comprising pancreas cells.

99. A method of claim 98, further comprising assessing the expression levels of a plurality of said genes or polypeptides.

25

100. A method for identifying an agent that modulates the expression of TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785, or the biological activity of a polypeptide encoded thereby, comprising,

contacting a pancreas cell with a test agent under conditions effective for said test 30 agent to modulate the expression of TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785 of claim 113, or the biological activity of a polypeptide encoded thereby, in said

pancreas cell, and

determining whether said test agent modulates said gene or polypeptide.

101. A method of claim 100, wherein said agent is an antisense polynucleotide to a target

5 polynucleotide sequence selected from SEQ ID NO 152, 162, 167, 171, or 175 and which is effective to inhibit translation of said gene.

102. A method of detecting polymorphisms in TMD0986, XM_061780, XM_061781,

XM_061784, or XM_061785, comprising,

10 comparing the structure of: genomic DNA or RNA or cDNA comprising all or part of an allele of TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785,

with SEQ ID NOS 152, 153, 162, 163, 167, 168, 171, 172, 175, or 176 of claim 113.

103. A method of claim 102, wherein said polymorphism is a nucleotide deletion,

15 substitution, inversion, or transposition.

104. A method of identifying a pancreatic disease or pancreatic disease-susceptibility,

comprising:

determining the association of a pancreatic disease or pancreatic disease-susceptibility

20 with a nucleotide sequence present within the pancreatic gene complex of claim 113.

105. A method of claim 104, wherein the pancreatic gene complex is from LOC160025-

LOC119954.

106. A method of claim 104, wherein determining is performed by producing a human-

25 linkage map of said complex.

107. A method of claim 104, wherein determining is performed by comparing the

nucleotide sequences between normal subjects and subjects having a pancreas disorder.

30 108. A non-human, transgenic mammal whose genome comprises a functional disruption of

a gene represented by TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785

of claim 113, and which has a defect in pancreas function.

109. A mammalian pancreas cell whose genome comprises a functional disruption of a gene represented by TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785 of claim
5 113, and which has a defect in pancreas function.

110. A mammalian cell of claim 109, wherein said cell is a mouse cell.

111. A pancreas cell, comprising a gene operatively linked to an expression control sequence
10 effective to express said gene in pancreas, wherein said sequence is SEQ ID NOS 156-161,
179, or 180.

112. A method of selecting a gene predominantly expressed in pancreas cells from a
database comprising polynucleotide sequences for genes, comprising:

15 displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide
sequence for TMD0986, XM_061780, XM_061781, XM_061784, or XM_061785 of claim
113, or complements to the polynucleotides sequence,

wherein said displayed sequences have been retrieved from said database upon
selection by a user.

20

113. A composition comprising: a pancreas specific gene consisting essentially of
TMD0986, XM_061780, XM_061781, XM_061784, and/or XM_061785, or a polypeptide
encoded thereby.

25 114. An isolated polynucleotide comprising a polynucleotide sequence which codes without
interruption for a human TMD0986 having an amino acid sequence set forth in SEQ ID NO
153, or a complement thereto.

115. An isolated polynucleotide comprising,

30 a human TMD0986 polynucleotide sequence having 90% or more nucleotide
sequence identity to the polynucleotide sequence set forth in SEQ ID NO 152 along its entire

length, which codes without interruption for human TMD0986, or a complement thereto, and which has G-protein coupling activity.

116. An isolated humansTMD0986 polypeptide comprising the amino acid sequence of a

5 human TMD0986 as set forth in SEQ ID NO 153.

117. An isolated human TMD0986 polypeptide consisting essentially of amino acids 1-117 of a human TMD0986 as set forth in SEQ ID NO 153.

10 118. An isolated polypeptide which is human TMD0986 having 90% or more amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO 153, and which has protein binding activity.

119. An antibody specific for an epitope selected from the polypeptide of claim 117.

15 120. A method of detecting an retinal cell, comprising:

contacting a sample comprising cells with a polynucleotide specific for NM_013941 (SEQ ID NO 181), or a naturally-occurring polymorphisms thereof, of claim 142 under conditions effective for said polynucleotide to hybridize specifically to said gene, and

20 detecting specific hybridization.

121. A method of claim 120, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

25

122. A method of detecting an retinal cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for by NM_013941 (SEQ ID NO 182), or a naturally-occurring polymorphism thereof, of claim 142 under conditions effective for said binding partner bind specifically to said

30 polypeptide, and

detecting specific binding.

123. A method of claim 122, wherein said detecting is performed by:
immunocytochemistry, immunoprecipitation, or Western blot.

124. A method of delivering an agent to a retinal cell, comprising:
5 contacting a retinal cell with an agent coupled to binding partner specific for by
NM_013941 (SEQ ID NO 182), or naturally-occurring polymorphism thereof, of claim 142,
whereby said agent is delivered to said cell.

125. A method of claim 124, wherein the agent is a therapeutic agent or an imaging agent.
10

126. A method of claim 124, wherein the agent is cytotoxic.

127. A method of claim 124, wherein the binding partner is an antibody.

15 128. A method of modulating a retinal cell, comprising:
contacting said cell with an agent effective to modulate NM_013941 (SEQ ID NO
181 or 182), or the biological activity of a polypeptide encoded thereby, of claim 142,
whereby the retinal cell is modulated.

20 129. A method of diagnosing a retinal disease associated with abnormal gene expression, or
determining a subject's susceptibility to such disease, comprising:
assessing the expression of NM_013941, a polymorphism thereof, or polypeptide
encoded thereby, of claim 142 in a tissue sample comprising retinal cells.

25 130. A method of claim 129, wherein assessing is:
measuring expression levels of said gene, determining the genomic structure of said
gene, determining the mRNA structure of transcripts from said gene, or measuring the
expression levels of polypeptide coded for by said gene.

30 131. A method of claim 129, wherein said assessing detecting is performed by:
Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR,

RACE PCR, or *in situ* hybridization, and
using a polynucleotide probe having a sequence selected from SEQ ID NOS 183 or
184, or a complement thereto.

- 5 132. A method of assessing a therapeutic or preventative intervention in a subject having an
retinal disease, comprising,
 determining the expression levels of NM_013941, a polymorphism thereof, or
polypeptide encoded thereby, of claim 142 in a tissue sample comprising retinal cells.
- 10 133. A method of claim 132, further comprising assessing the expression levels of a plurality
of said genes or polypeptides.
134. A method for identifying an agent that modulates the expression of NM_013941 or the
biological activity of a polypeptide encoded thereby, comprising,
 contacting an retinal cell with a test agent under conditions effective for said test
15 agent to modulate the expression of NM_013941 or a polymorphism thereof, of claim 142, or
the biological activity of a polypeptide encoded thereby, in said retinal cell, and
 determining whether said test agent modulates said gene or polypeptide.
135. A method of claim 134, wherein said agent is an antisense polynucleotide to a target
20 polynucleotide sequence selected from SEQ ID NO 181 and which is effective to inhibit
translation of said gene.
136. A method of detecting polymorphisms in NM_013941, comprising:
 comparing the structure of: genomic DNA or RNA or cDNA comprising all or part
25 of an allele of NM_013941, with SEQ ID NOS 181 or 182 of claim 142.
137. A method of claim 136, wherein said polymorphism is a nucleotide deletion,
substitution, inversion, or transposition.
- 30 138. A non-human, transgenic mammal whose genome comprises a functional disruption of
a gene represented by NM_013941 (SEQ ID NO 181) of claim 142, and which has a defect in

retinal function.

139. A mammalian retinal cell whose genome comprises a functional disruption of a gene represented by NM_013941 (SEQ ID NO 181) of claim 142, and which has a defect in retinal
5 function.

140. A mammalian cell of claim 139, wherein said cell is a mouse cell.

141. A method of selecting a gene predominantly expressed in retinal cells from a database
10 comprising polynucleotide sequences for genes, comprising:

displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide sequence for NM_013941 (SEQ ID NO 181 or 182) of claim 142, or complements to the polynucleotides sequence,

15 wherein said displayed sequences have been retrieved from said database upon selection by a user.

142. A composition comprising:

a retinal specific gene consisting essentially of NM_013941 (SEQ ID NO 181 or 182), or a polypeptide encoded thereby.

20 143. A method of detecting a spleen cell, comprising:

contacting a sample comprising cells with a polynucleotide specific for TMD1030 (XM_166853) or TMD0621 (XM_166205) of claim 170 under conditions effective for said polynucleotide to hybridize specifically to said gene, and

25 detecting specific hybridization.

144. A method of claim 143, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

30 145. A method of detecting a spleen cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide

coded for by TMD1030 (XM_166853) or TMD0621 (XM_166205) of claim 170 under conditions effective for said binding partner bind specifically to said polypeptide, and detecting specific binding.

5 146. A method of claim 145, wherein said detecting is performed by:
immunocytochemistry, immunoprecipitation, or Western blot.

147. A method of delivering an agent to a spleen cell, comprising:
contacting a spleen with an agent coupled to binding partner specific for TMD1030
10 (XM_166853) or TMD0621 (XM_166205) of claim 170, whereby said agent is delivered to
said cell.

148. A method of claim 147, wherein the agent is a therapeutic agent or an imaging agent.

15 149. A method of claim 148, wherein the agent is cytotoxic.

150. A method of claim 147, wherein the binding partner is an antibody.

151. A method of modulating a spleen, immune, or reticuloendothelial cell, comprising:
20 contacting said cell with an agent effective to modulate TMD1030 (XM_166853),
TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), or the
biological activity of a polypeptide encoded thereby, of claim 170, whereby the cell is
modulated.

25 152. A method of assessing spleen function, comprising:
detecting a polypeptide coded for by TMD1030 (XM_166853) or TMD0621
(XM_166205) of claim 170, or fragments thereof, in a body fluid, whereby the amount of
said polypeptide in said fluid is a measure of spleen function.

30 153. A method of claim 152, wherein said detecting is performed using an antibody which is
specific for said polypeptide.

154. A method of claim 152, wherein said detecting is performed by RIA, ELISA, or Western blot.

5 155. A method of expressing a heterologous polynucleotide in spleen cells, comprising:
expressing a nucleic acid construct in spleen cell, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is SEQ ID NO 205-213.

10 156. A method of assessing a therapeutic or preventative intervention in a subject having a spleen or lymphoid disease, comprising,
determining the expression levels of TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), or a polypeptide encoded thereby, of claim 170 in a tissue sample comprising spleen, lymphoid, or
15 reticuloendothelial cells.

157. A method of claim 156, further comprising assessing the expression levels of a plurality of said genes or polypeptides.

20 158. A method for identifying an agent that modulates the expression of TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), comprising,
contacting a spleen, lymphoid, or reticuloendothelial cell, with a test agent under conditions effective for said test agent to modulate the expression of TMD1030
25 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), of claim 170, and
determining whether said test agent modulates said gene.

159. A method of claim 158, wherein said agent is an antisense which is effective to inhibit
30 translation of said gene.

160. A method for identifying an agent that modulates the expression of a polypeptide coded for by TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), comprising,

5 contacting a polypeptide coded for by TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205) of claim 170, with a test agent under conditions effective for said test agent to modulate said polypeptide, and determining whether said test agent modulates said polypeptide.

161. A method of detecting polymorphisms in comprising, comparing the structure of :
10 genomic DNA or RNA or cDNA comprising all or part of an allele of TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205), with SEQ ID NOS 185, 187, 189, or 191 of claim 170.

162. A method of claim 161, wherein said polymorphism is a nucleotide deletion,
15 substitution, inversion, or transposition.

163. A method of identifying a genetic basis for a spleen, lymphoid, and/or reticuloendothelial disease or disease-susceptibility, comprising: determining the association of a spleen, lymphoid, and/or reticuloendothelial disease or disease-susceptibility with a
20 nucleotide sequence present in the gene complex of claim 170.

164. A method of claim 163, wherein determining is performed by producing a human-linkage map of said complex.

25 165. A method of claim 163, wherein determining is performed by comparing the nucleotide sequences between normal subjects and subjects having a spleen, lymphoid, and/or reticuloendothelial disease.

166. A non-human, transgenic mammal, or a cell thereof. whose genome comprises a
30 functional disruption of a gene represented by TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205) of claim 170, and

which has a defect in spleen, lymphoid, and/or reticuloendothelial disease function.

167. A mammalian cell of claim 166, wherein said cell is a mouse cell.

5 168. A spleen, lymphoid, and/or reticuloendothelial cell, comprising a gene operatively linked to an expression control sequence effective to express said gene in spleen, lymphoid, and/or reticuloendothelial, wherein said sequence is SEQ ID NO 205-213.

10 169. A method of selecting a gene predominantly expressed in spleen, lymphoid, and/or reticuloendothelial cells from a database comprising polynucleotide sequences for genes, comprising:

displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide sequence for TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), or TMD0621 (XM_166205) of claim 170, or complements to the

15 170. polynucleotides sequence, wherein said displayed sequences have been retrieved from said database upon selection by a user.

170. A composition consisting essentially of the 11q12.2 spleen gene complex, comprising TMD1030 (XM_166853), TMD1029 (XM_166854), TMD1028 (XM_166855), and 20 TMD0621 (XM_166205).

171. A composition of claim 170, wherein said complex consists essentially of the chromosome region between STS markers G62658 and SHGC-154002.

25 172. A method of detecting a pancreas cell, comprising:

contacting a sample comprising cells with a polynucleotide specific TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127 of claim 199 30 under conditions effective for said polynucleotide to hybridize specifically to said gene, and detecting specific hybridization.

173. A method of claim 172, wherein said detecting is performed by:

Northern blot analysis, polymerase chain reaction (PCR), reverse transcriptase PCR, RACE PCR, or *in situ* hybridization.

5 174. A method of detecting a pancreas cell, comprising:

contacting a sample comprising cells with a binding partner specific for a polypeptide coded for by TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or

10 TMD1127

of claim 199 under conditions effective for said binding partner bind specifically to said polypeptide, and

detecting specific binding.

15 175. A method of claim 174, wherein said detecting is performed by:

immunocytochemistry, immunoprecipitation, or Western blot.

176. A method of delivering an agent to a pancreas cell, comprising:

contacting a pancreas with an agent coupled to binding partner specific for
20 TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127 of claim 199, whereby said agent is delivered to said cell.

25 177. A method of claim 176, wherein the agent is a therapeutic agent or an imaging agent.

178. A method of claim 176, wherein the agent is cytotoxic.

179. A method of claim 176, wherein the binding partner is an antibody.

30

180. A method of modulating a pancreas, immune, or reticuloendothelial cell, comprising:

contacting said cell with an agent effective to modulate TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, or the biological activity of 5 a polypeptide encoded thereby, of claim 199, whereby the cell is modulated.

181. A method of assessing pancreas function, comprising:

detecting a polypeptide coded for by TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, 10 TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127 of claim 199, or fragments thereof, in a body fluid, whereby the amount of said polypeptide in said fluid is a measure of pancreas function.

182. A method of claim 181, wherein said detecting is performed using an antibody which is specific for said polypeptide.

15

183. A method of claim 181, wherein said detecting is performed by RIA, ELISA, or Western blot.

184. A method of expressing a heterologous polynucleotide in pancreas cells, comprising:

20 expressing a nucleic acid construct in pancreas cell, said construct comprising a promoter sequence operably linked to said heterologous polynucleotide, wherein said promoter sequence is selected SEQ ID NO 258, 261, 262, 265-267, 270-272, 275, 278, 279, 282-284, 287, 290-293, 296, 297, 300, 303, 306, 309-314, 317-320, 323-326, 329, 332-333, 336-338, 341, and 344.

25

185. A method of assessing a therapeutic or preventative intervention in a subject having a pancreas or lymphoid disease, comprising,

determining the expression levels of TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, 30 TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, or a polypeptide encoded thereby, of claim 199 in

a tissue sample comprising pancreas, lymphoid, or reticuloendothelial cells.

186. A method of claim 185, further comprising assessing the expression levels of a plurality of said genes or polypeptides.

5

187. A method for identifying an agent that modulates the expression of TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, comprising,

10 contacting a pancreas, lymphoid, or reticuloendothelial cell, with a test agent under conditions effective for said test agent to modulate the expression of TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, of claim 199, and

15 determining whether said test agent modulates said gene.

188. A method of claim 187, wherein said agent is an antisense which is effective to inhibit translation of said gene.

20 189. A method for identifying an agent that modulates the expression of a polypeptide coded for by TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, comprising,

25 contacting a polypeptide coded for by TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127 of claim 199, with a test agent under conditions effective for said test agent to modulate said polypeptide, and

30 determining whether said test agent modulates said polypeptide.

190. A method of claim 189, wherein said test agent is an antibody.
191. A method of detecting polymorphisms in comprising, comparing the structure of :
genomic DNA or RNA or cDNA comprising all or part of an allele of
5 TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290,
TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674, TMD0675,
TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127,
with SEQ ID NOS of Table 23 of claim 199.
- 10 192. A method of claim 191, wherein said polymorphism is a nucleotide deletion,
substitution, inversion, or transposition.
193. A method of identifying a genetic basis for a pancreas disease or disease-susceptibility,
comprising: determining the association of a pancreas disease or disease-susceptibility with a
15 gene of claim 199.
194. A method of claim 193, wherein determining is performed by producing a human-
linkage map of said gene.
- 20 195. A method of claim 193, wherein determining is performed by comparing the
nucleotide sequences between normal subjects and subjects having a pancreas disease.
196. A non-human, transgenic mammal, or a cell thereof, whose genome comprises a
functional disruption of a gene represented by TMD0077, TMD0233, TMD0256, TMD0258,
25 TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639,
TMD0645, TMD0674, TMD0675, TMD0677, TMD0726, TMD0727, TMD0739,
TMD0753, TMD1111, and/or TMD1127, of claim 199, and which has a defect in pancreas,
lymphoid, and/or reticuloendothelial disease function.
- 30 197. A mammalian cell of claim 196, wherein said cell is a mouse cell.
198. A method of selecting a gene predominantly expressed in pancreas tissue from a

database comprising polynucleotide and amino acid sequences for genes, comprising:

displaying, in a computer-readable medium, a polynucleotide sequence or polypeptide sequence for TMD0077, TMD0233, TMD0256, TMD0258, TMD0267, TMD0271, TMD0290, TMD0530, TMD0574, TMD0608, TMD0639, TMD0645, TMD0674,

5 TMD0675, TMD0677, TMD0726, TMD0727, TMD0739, TMD0753, TMD1111, and/or TMD1127, of claim 199, or complements to the polynucleotides sequence, wherein said displayed sequences have been retrieved from said database upon selection by a user.

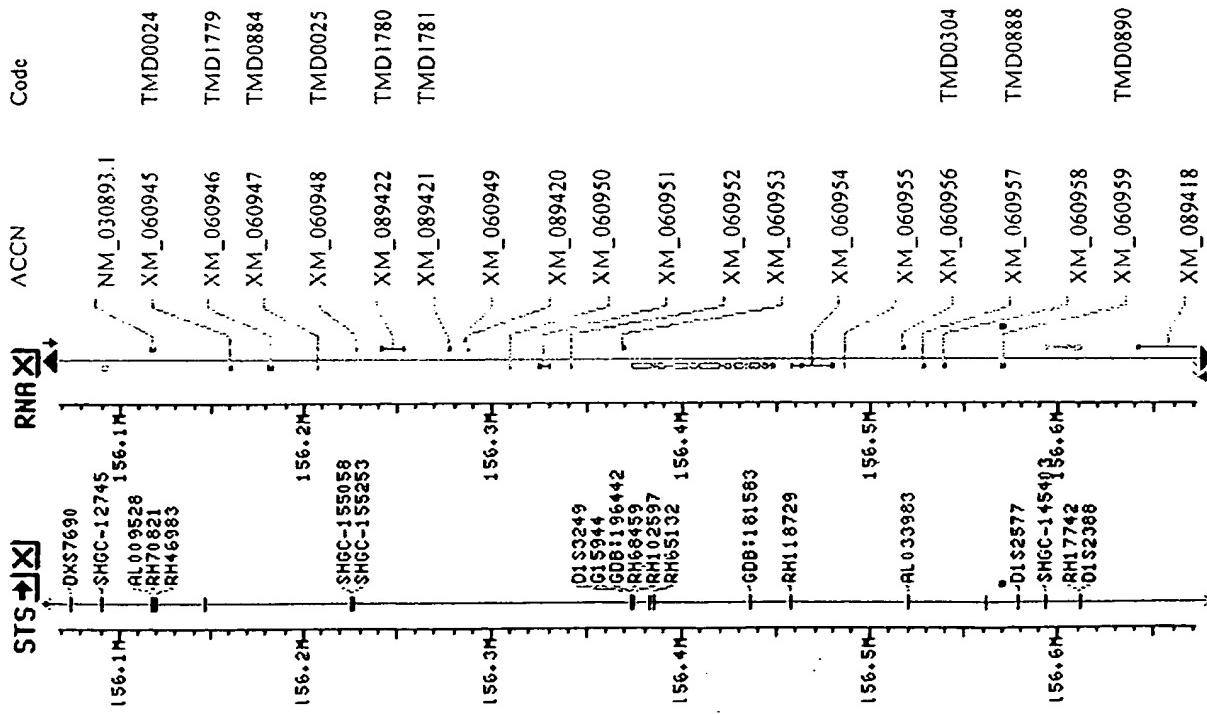
199. A composition comprising genes and/or polypeptide which are expressed

10 predominantly in pancreas tissue comprising:

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Fig. 1

**Fig. 2**

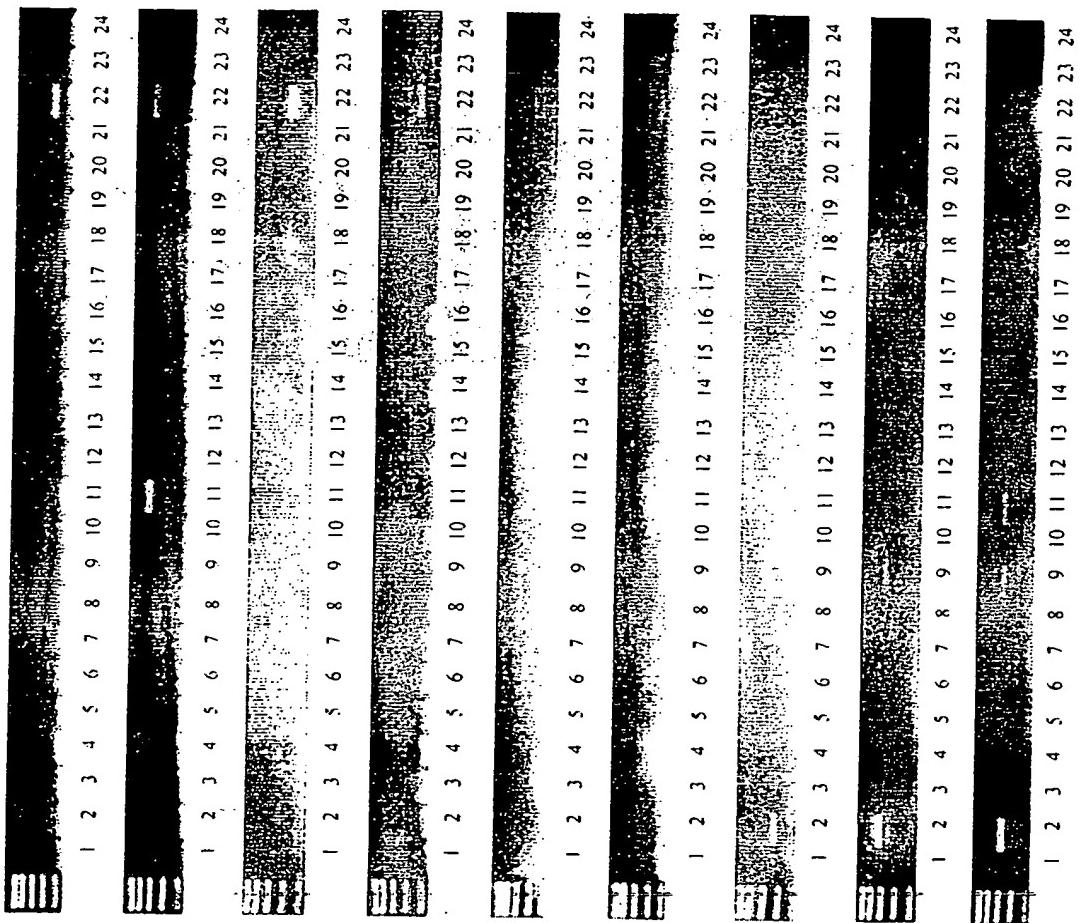
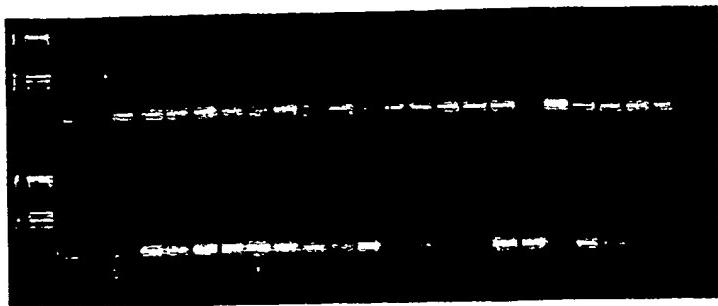


Fig. 3

XM_062147



XM_061676

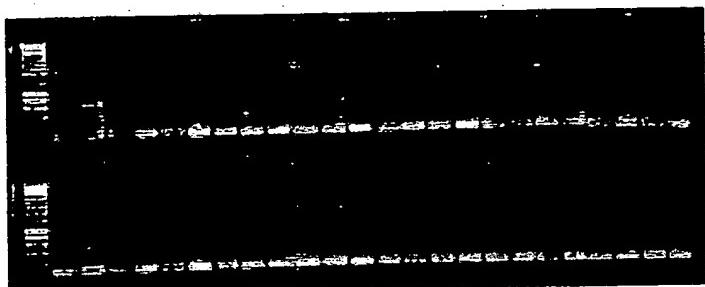


FIG. 4

Fig. 5a

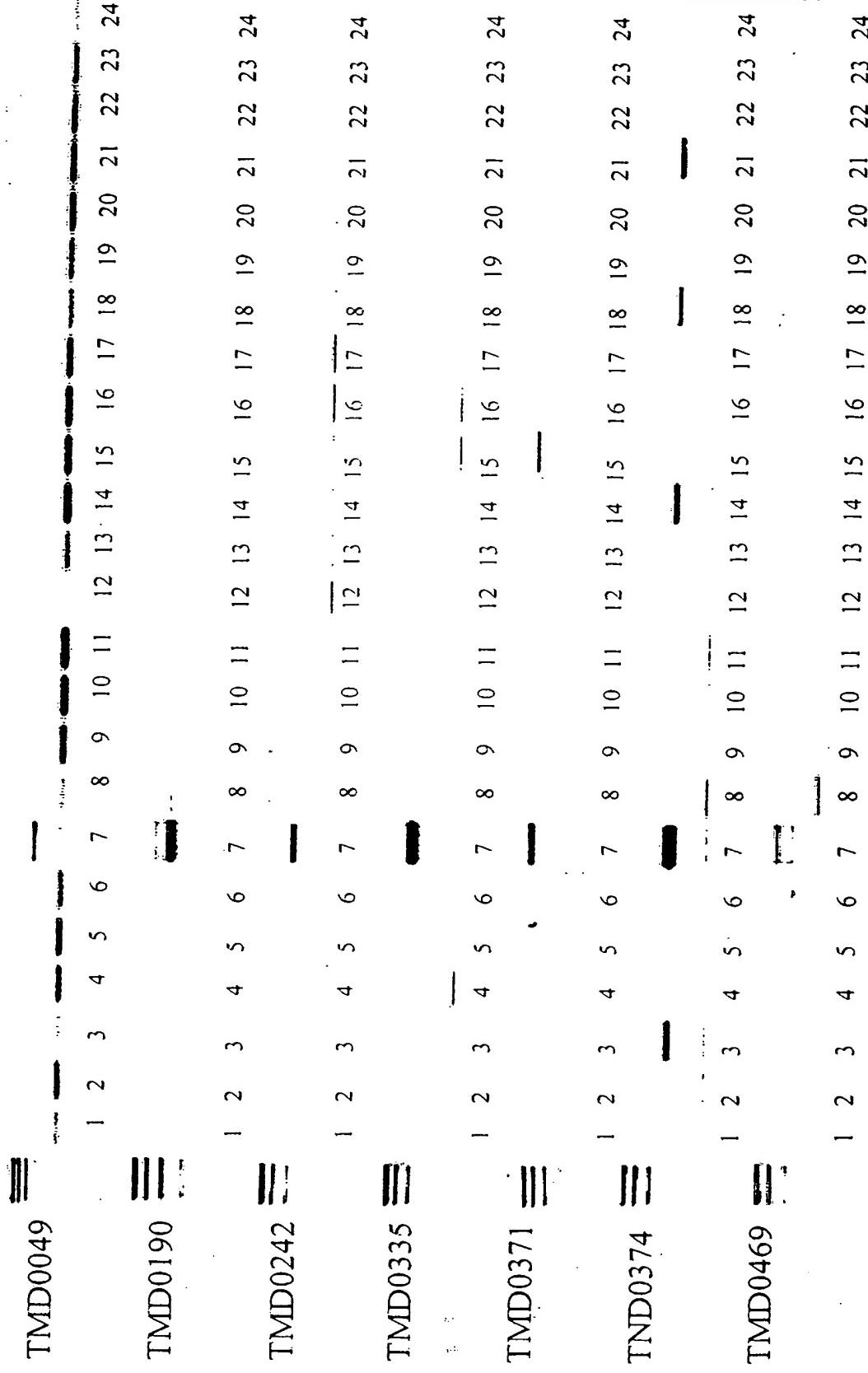
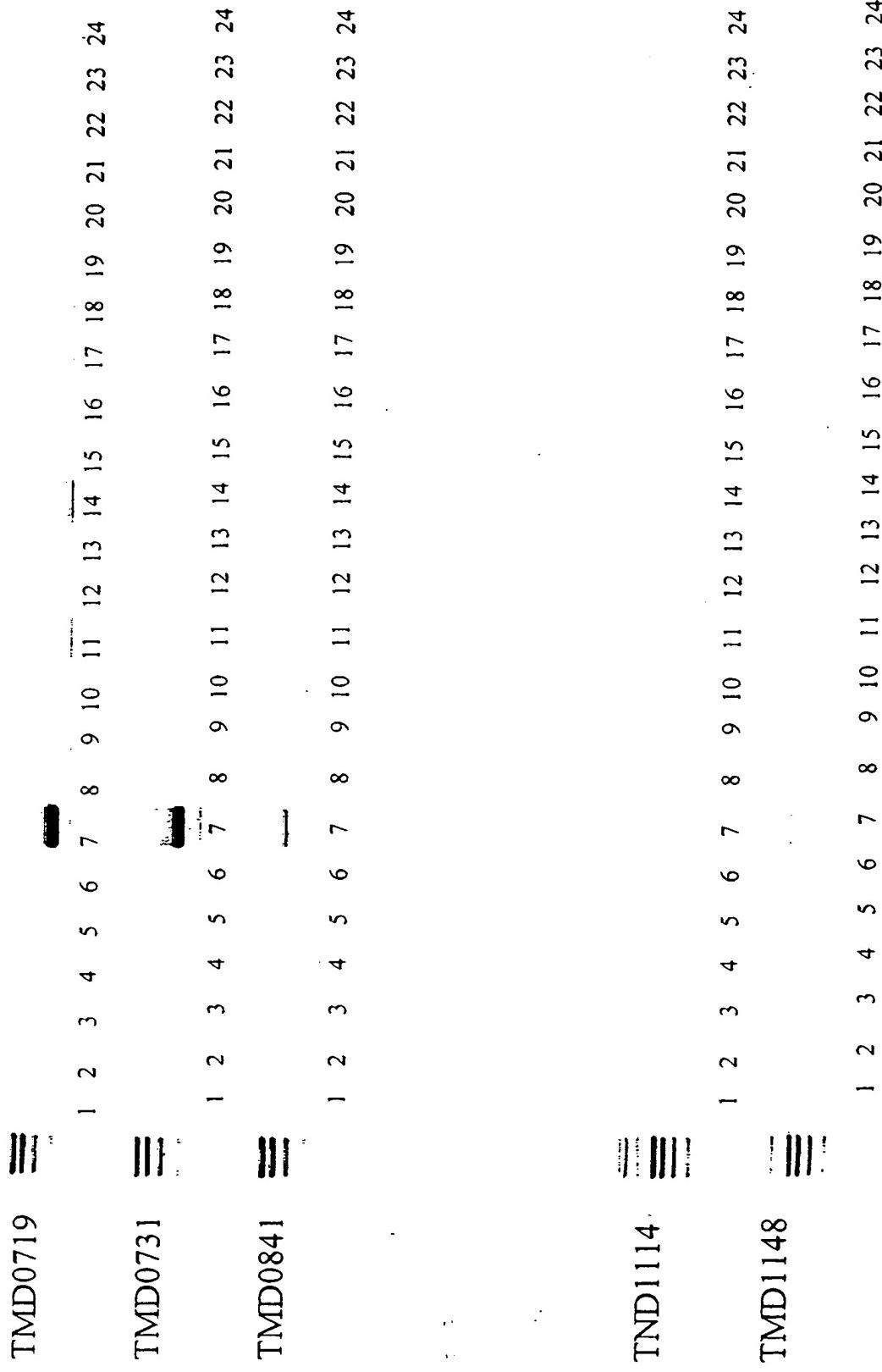


Fig. 5b



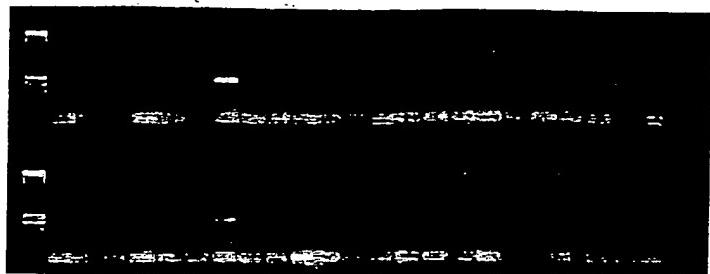


Fig. 6

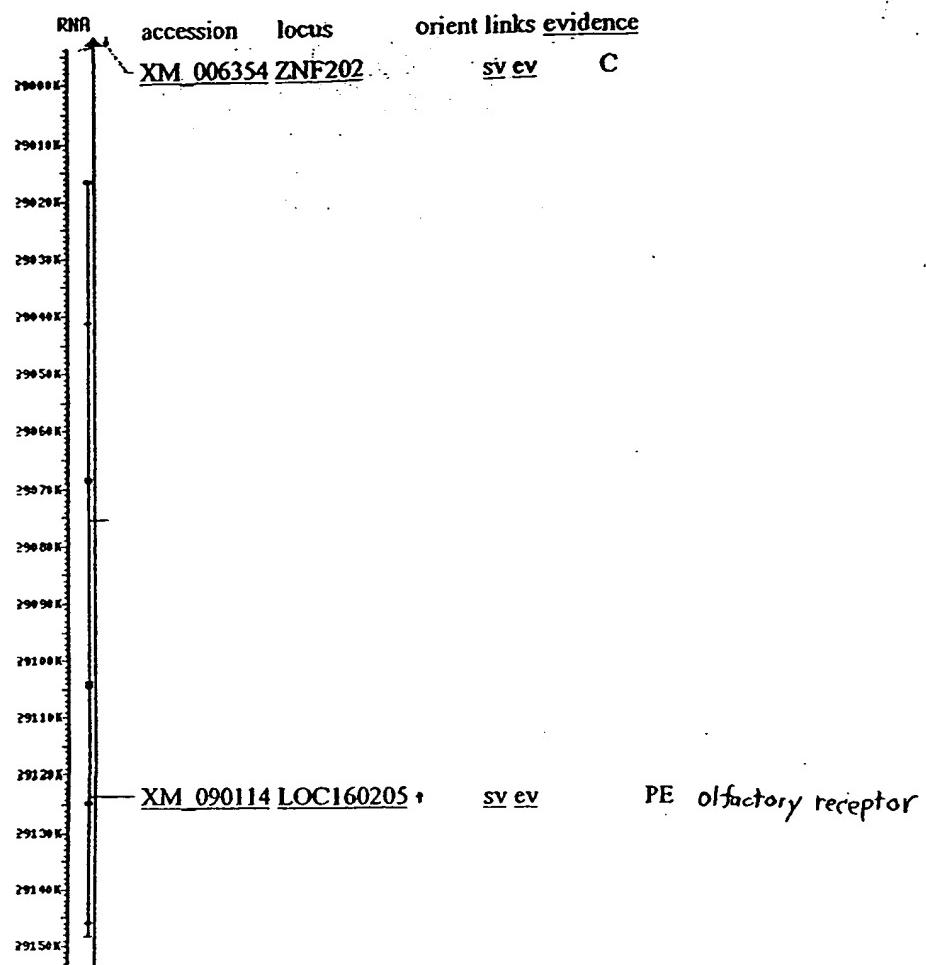


Fig EA

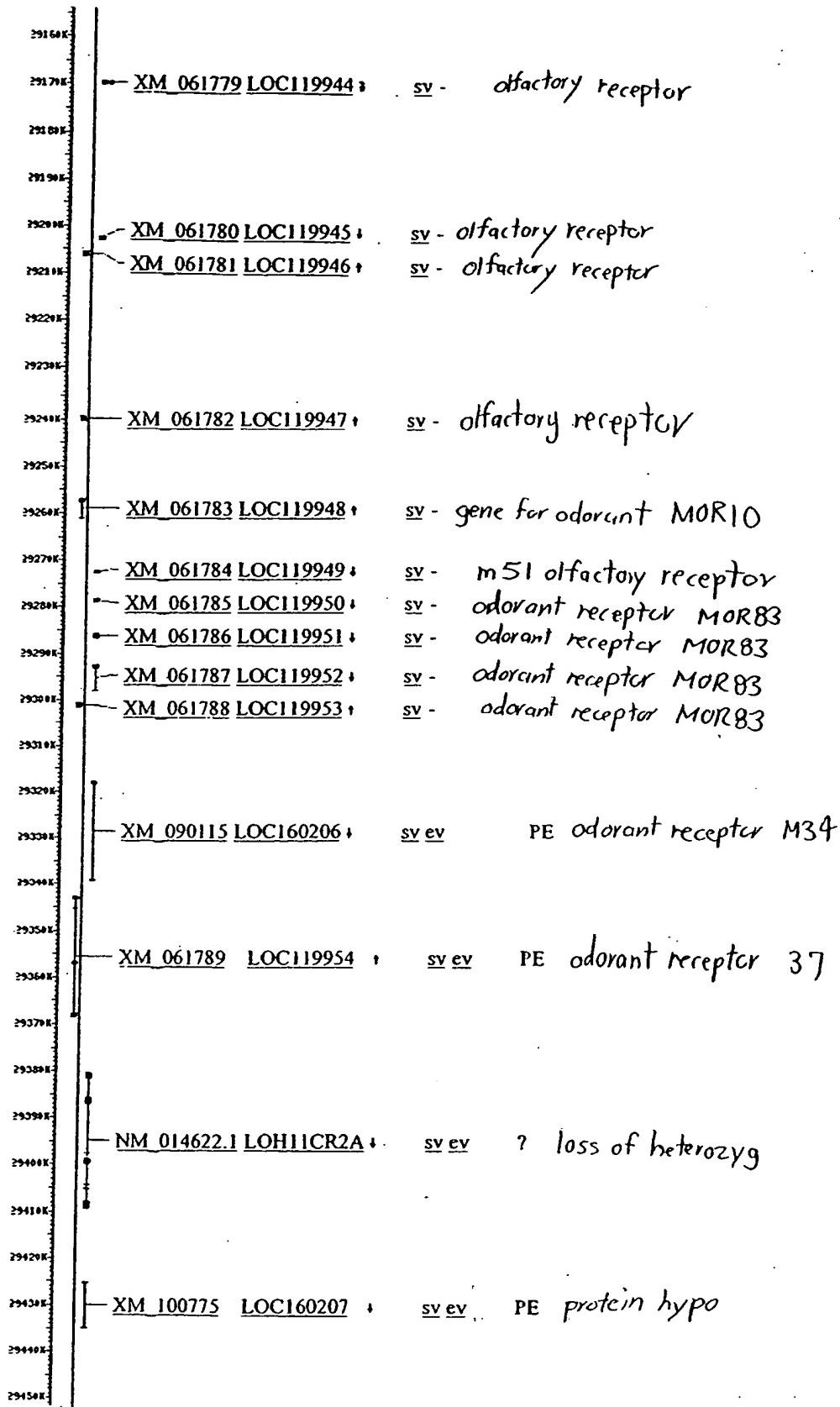


Fig 1B

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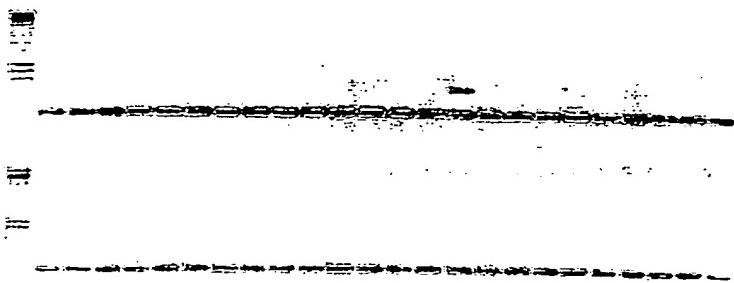
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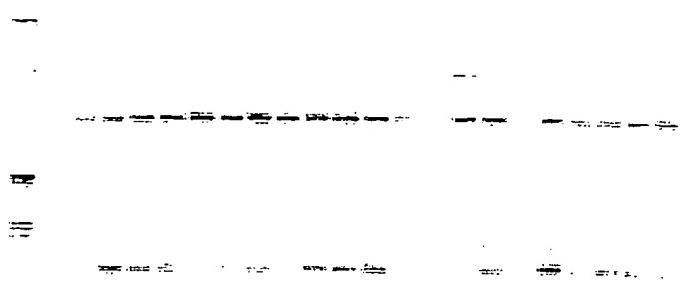
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Fig. 8

XM_061779



XM_061780



XM_061781

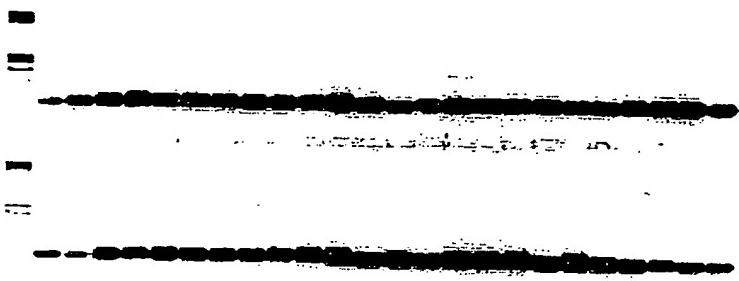
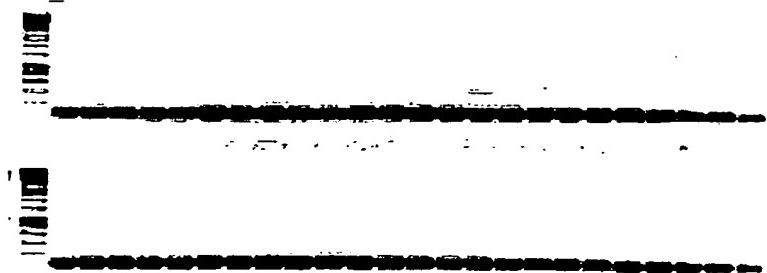


Fig. 9A

XM_061784



XM_061785

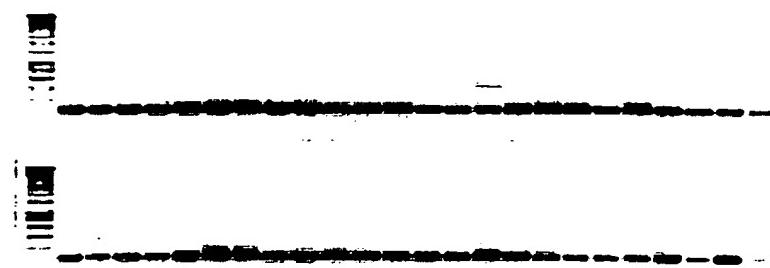


Fig. 9B

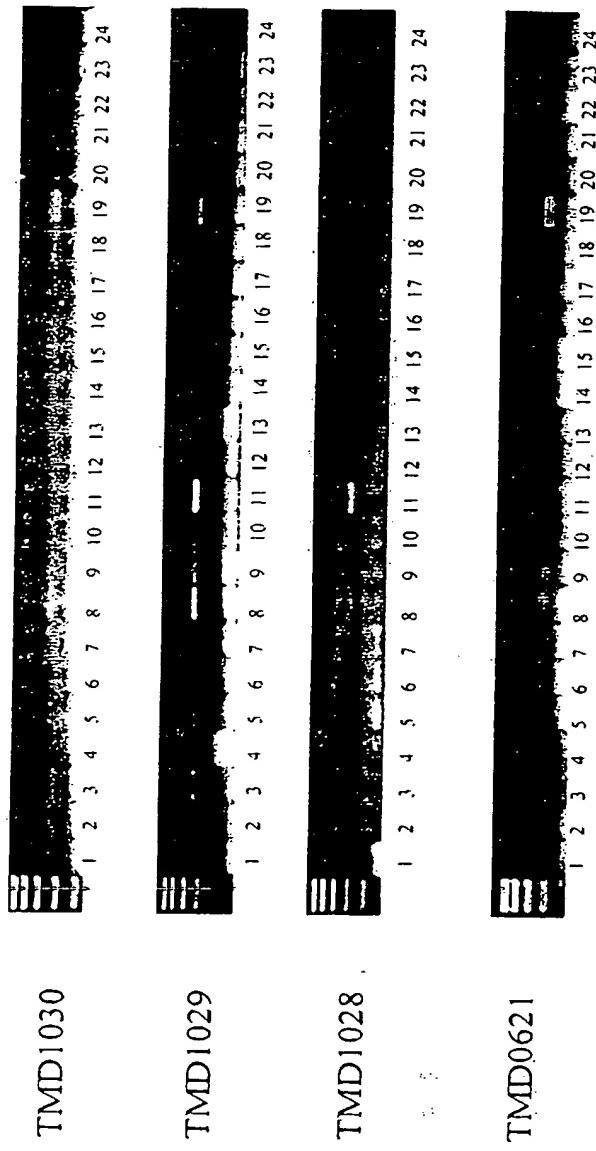


Fig.10

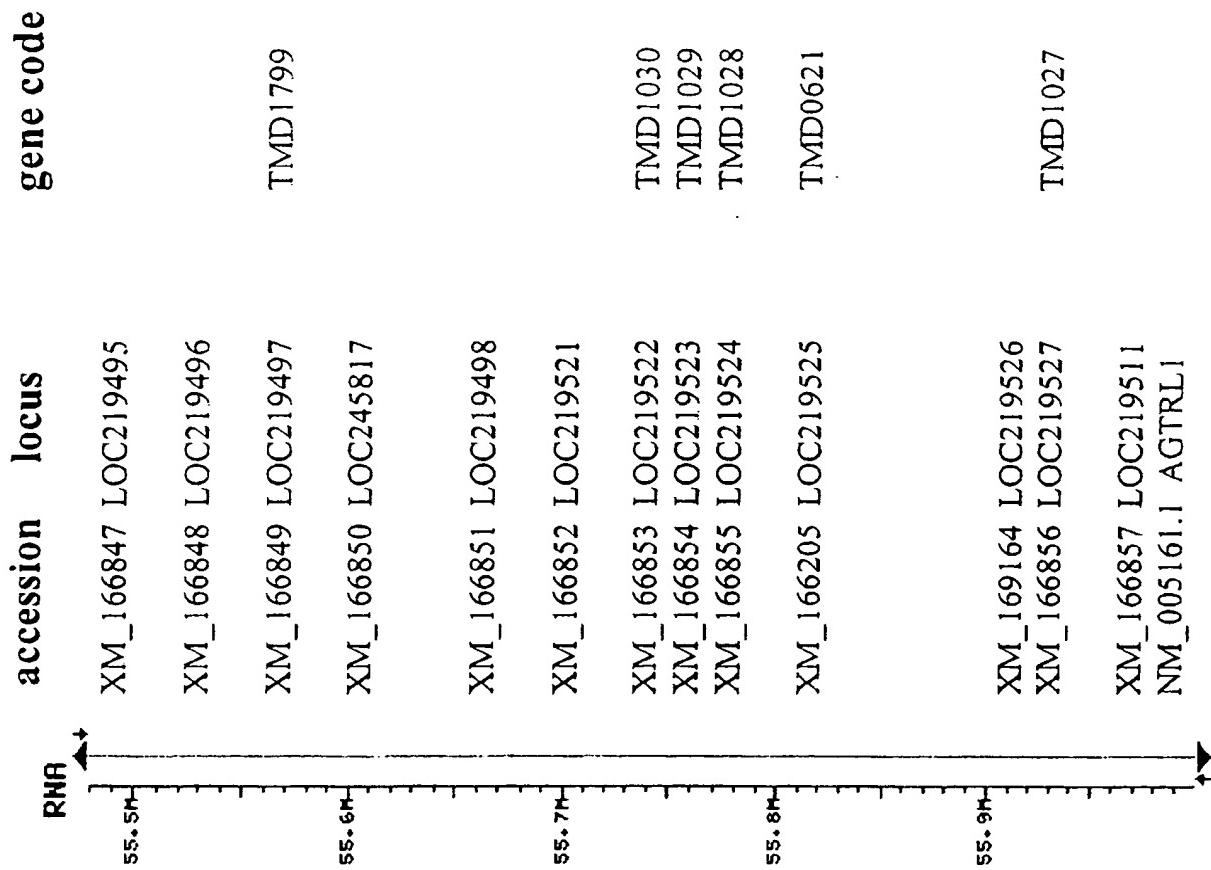


Fig. 11

FIG. 12A

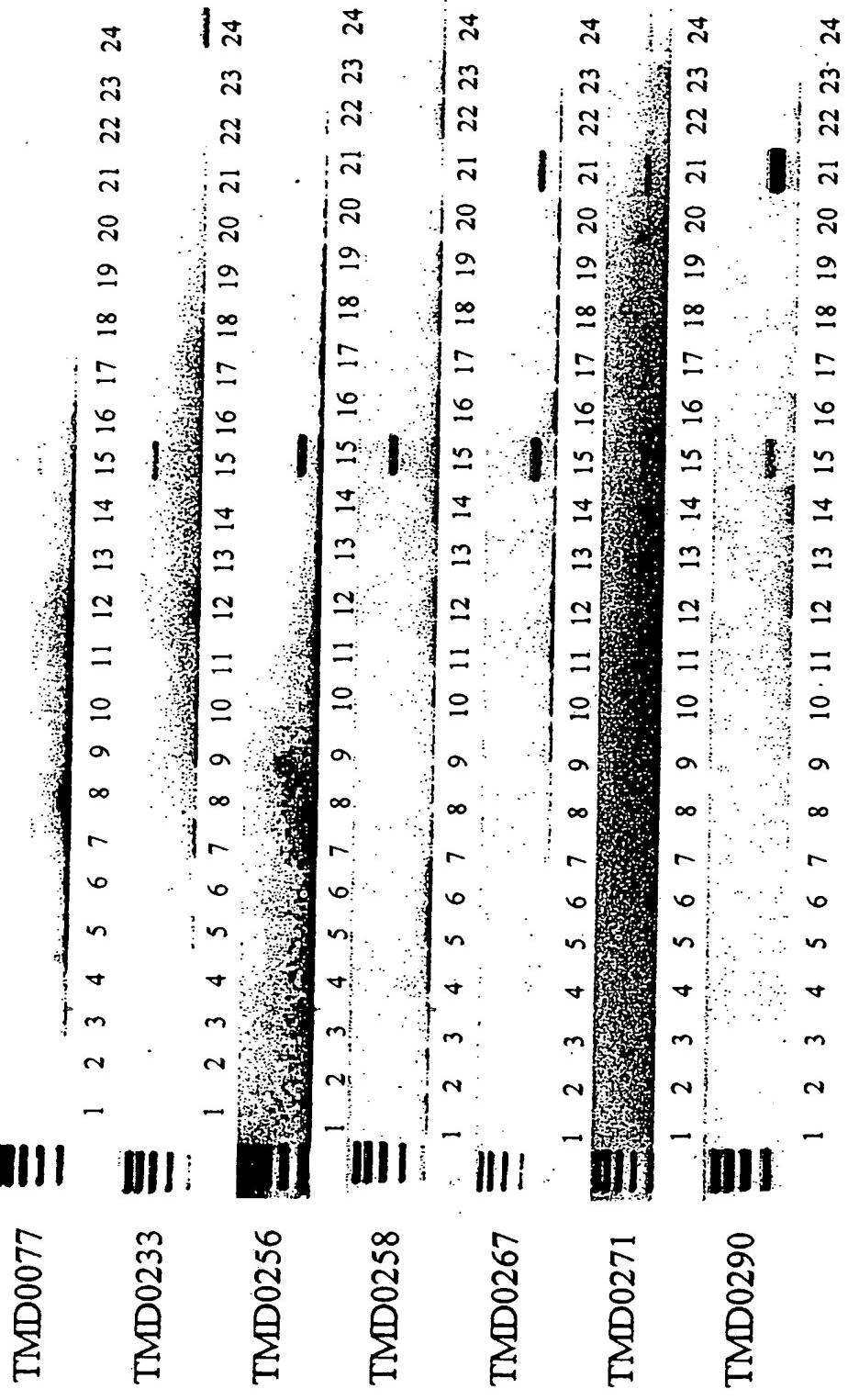


FIG. 12B

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| TMD0608 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0639 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0645 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0674 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0675 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |

FIG. 12C

| | |
|---------|--|
| TMD0677 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0726 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0727 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0739 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD0753 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
| TMD1111 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 |
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| Pro Val Leu Lys Leu Ala Ser Gln His Ser Gly Phe Ser Gln Leu Val | |
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4982

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Leu Leu Tyr Leu Phe Thr Leu Gly Thr Asn Ala Ile Ile Ser Thr
35 40 45

Ile Val Leu Asp Arg Ala Leu His Thr Pro Met Tyr Phe Phe Leu Ala
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Ile Leu Ser Cys Ser Glu Ile Cys Tyr Thr Phe Val Ile Val Pro Lys
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Met Leu Val Asp Leu Leu Ser Gln Lys Lys Thr Ile Ser Phe Leu Gly
85 90 95

Cys Ala Ile Gln Met Phe Ser Phe Leu Phe Phe Gly Ser Ser His Ser
100 105 110

Phe Leu Leu Ala Ala Met Gly Tyr Asp Arg Tyr Met Ala Ile Cys Asn
115 120 125

Pro Leu Arg Tyr Ser Val Leu Met Gly His Gly Val Cys Met Gly Leu
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Met Ala Ala Ala Cys Ala Cys Gly Phe Thr Val Ser Leu Val Thr Thr
145 150 155 160

Ser Leu Val Phe His Leu Pro Phe His Ser Ser Asn Gln Leu His His
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Phe Phe Cys Asp Ile Ser Pro Val Leu Lys Leu Ala Ser Gln His Ser
180 185 190

Gly Phe Ser Gln Leu Val Ile Phe Met Leu Gly Val Phe Ala Leu Val
195 200 205

Ile Pro Leu Leu Ile Leu Val Ser Tyr Ile Arg Ile Ile Ser Ala
210 215 220

Ile Leu Lys Ile Pro Ser Ser Val Gly Arg Tyr Lys Thr Phe Ser Thr
225 230 235 240

Cys Ala Ser His Leu Ile Val Val Thr Val His Tyr Ser Cys Ala Ser
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Phe Ile Tyr Leu Arg Pro Lys Thr Asn Tyr Thr Ser Ser Gln Asp Thr
260 265 270

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| att ccc ttg ctt ctc atc tac gga ttt atc cta act gga aac cta ata Ile Pro Leu Leu Ile Tyr Gly Phe Ile Leu Thr Gly Asn Leu Ile | 35 | 40 | 45 | 144 |
| atg ttc att gtc atc cag gtg ggc atg gcc ctg cac acc cct ttg tat Met Phe Ile Val Ile Gln Val Gly Met Ala Leu His Thr Pro Leu Tyr | 50 | 55 | 60 | 192 |
| ttc ttt atc agt gtc ctc tcc ttc ctg gag atc tgc tat acc aca acc Phe Phe Ile Ser Val Leu Ser Phe Leu Glu Ile Cys Tyr Thr Thr Thr | 65 | 70 | 75 | 240 |
| acc atc ccc aag atg ctg tcc tgc cta atc agt gag cag aag agc att Thr Ile Pro Lys Met Leu Ser Cys Leu Ile Ser Glu Gln Lys Ser Ile | 85 | 90 | 95 | 288 |
| tcc gtg gct ggc tgc ctc ctg cag atg tac ttt ttc cac tca ctt ggt Ser Val Ala Gly Cys Leu Leu Gln Met Tyr Phe Phe His Ser Leu Gly | 100 | 105 | 110 | 336 |
| atc aca gaa agc tgt gtc ctg aca gca atg gcc att gac agg tac ata Ile Thr Glu Ser Cys Val Leu Thr Ala Met Ala Ile Asp Arg Tyr Ile | 115 | 120 | 125 | 384 |
| gct atc tgc aat cca ctc cgt tac cca acc atc atg att ccc aaa ctt Ala Ile Cys Asn Pro Leu Arg Tyr Pro Thr Ile Met Ile Pro Lys Leu | 130 | 135 | 140 | 432 |
| tgt atc cag ctg aca gtt gga tcc tgc ttt tgt ggc ttc ctc ctt gtg Cys Ile Gln Leu Thr Val Gly Ser Cys Phe Cys Gly Phe Leu Leu Val | 145 | 150 | 155 | 480 |
| ctt cct gag att gca tgg att tcc acc ttg cct ttc tgt ggc tcc aac Leu Pro Glu Ile Ala Trp Ile Ser Thr Leu Pro Phe Cys Gly Ser Asn | 165 | 170 | 175 | 528 |
| cag atc cac cag ata ttc tgt gat ttc aca cct gtg ctg agc ttg gcc Gln Ile His Gln Ile Phe Cys Asp Phe Thr Pro Val Leu Ser Leu Ala | 180 | 185 | 190 | 576 |
| tgc aca gat aca ttc cta gtg gtc att gtg gat gcc atc cat gca gcg Cys Thr Asp Thr Phe Leu Val Val Ile Val Asp Ala Ile His Ala Ala | 195 | 200 | 205 | 624 |
| gaa att gta gcc tcc ttc ctg gtc att gct cta tcc tac atc cgg att Glu Ile Val Ala Ser Phe Leu Val Ile Ala Leu Ser Tyr Ile Arg Ile | 210 | 215 | 220 | 672 |
| att ata gtg att ctg gga atg cac tca gct gaa ggt cat cac aag gcc Ile Ile Val Ile Leu Gly Met His Ser Ala Glu Gly His His Lys Ala | 225 | 230 | 235 | 720 |
| ttt tcc acc tgt gct gct cac ctt gct gtg ttc ttg cta ttt ttt ggc Phe Ser Thr Cys Ala Ala His Leu Ala Val Phe Leu Leu Phe Phe Gly | 245 | 250 | 255 | 768 |
| agt gtg gct gtc atg tat ttg aga ttc tca gcc acc tac tca gtg ttt Ser Val Ala Val Met Tyr Leu Arg Phe Ser Ala Thr Tyr Ser Val Phe | 260 | 265 | 270 | 816 |
| tgg gac aca gca att gct gtc act ttt gtt atc ctt gct ccc ttt ttc Trp Asp Thr Ala Ile Ala Val Thr Phe Val Ile Leu Ala Pro Phe Phe | 275 | 280 | 285 | 864 |
| aac ccc atc atc tat agc ctg aaa aac aag gac atg aaa gag gct att Asn Pro Ile Ile Tyr Ser Leu Lys Asn Lys Asp Met Lys Glu Ala Ile | 290 | 295 | 300 | 912 |
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Met Phe Ile Val Ile Gln Val Gly Met Ala Leu His Thr Pro Leu Tyr
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Phe Phe Ile Ser Val Leu Ser Phe Leu Glu Ile Cys Tyr Thr Thr Thr
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Thr Ile Pro Lys Met Leu Ser Cys Leu Ile Ser Glu Gln Lys Ser Ile
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Ser Val Ala Gly Cys Leu Leu Gln Met Tyr Phe Phe His Ser Leu Gly
 100 105 110

Ile Thr Glu Ser Cys Val Leu Thr Ala Met Ala Ile Asp Arg Tyr Ile
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Ala Ile Cys Asn Pro Leu Arg Tyr Pro Thr Ile Met Ile Pro Lys Leu
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Cys Ile Gln Leu Thr Val Gly Ser Cys Phe Cys Gly Phe Leu Leu Val
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Leu Pro Glu Ile Ala Trp Ile Ser Thr Leu Pro Phe Cys Gly Ser Asn
 165 170 175

Gln Ile His Gln Ile Phe Cys Asp Phe Thr Pro Val Leu Ser Leu Ala
 180 185 190

Cys Thr Asp Thr Phe Leu Val Val Ile Val Asp Ala Ile His Ala Ala
 195 200 205

Glu Ile Val Ala Ser Phe Leu Val Ile Ala Leu Ser Tyr Ile Arg Ile
 210 215 220

Ile Ile Val Ile Leu Gly Met His Ser Ala Glu Gly His His Lys Ala
 225 230 235 240

Phe Ser Thr Cys Ala Ala His Leu Ala Val Phe Leu Leu Phe Phe Gly
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Ser Val Ala Val Met Tyr Leu Arg Phe Ser Ala Thr Tyr Ser Val Phe
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Trp Asp Thr Ala Ile Ala Val Thr Phe Val Ile Leu Ala Pro Phe Phe
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16U 200 PCT FINAL ST25
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Gln Ile Leu Leu Phe Phe Ile Phe Leu Leu Val Tyr Leu Thr Thr Leu
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His Thr Pro Met Tyr Phe Phe Leu Phe Val Leu Ser Cys Ser Glu Thr
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Cys Tyr Thr Leu Val Ile Val Pro Lys Met Leu Thr Asn Leu Leu Ser
65 70 75 80

gca att cca act att tct ttc tct gga tgt gtg gtc cag ctc tat tta 288
Ala Ilé Pro Thr Ile Ser Phe Ser Gly Cys Val Val Gln Leu Tyr Leu
85 90 95

ttt gtg ggc ttg gct tgt acc aac tgt ttt ctc att gct gtg atg ggc 336
Phe Val Gly Leu Ala Cys Thr Asn Cys Phe Leu Ile Ala Val Met Gly
100 105 110

tac gat cgc tat gtt gcc atc tgc aac ccc ctt aac tac aca ctc att 384
Tyr Asp Arg Tyr Val Ala Ile Cys Asn Pro Leu Asn Tyr Thr Leu Ile
115 120 125

ctg gtt cta gcc tcc agc ttt tgt ggc ttc ctg act tct gtg att gtc 432

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| Asn Ile Leu Val Phe Ser Val Leu Leu Cys Ala Ser Asn Arg Ile Asn | | | |
| 145 | 150 | 155 | 160 |
| cac ttt ttc tgt gac att tcc cct gtc ata aaa ctg ggc tgc aca gac | | | 528 |
| His Phe Phe Cys Asp Ile Ser Pro Val Ile Lys Leu Gly Cys Thr Asp | | | |
| 165 | 170 | 175 | |
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| Thr Asn Leu Lys Glu Met Val Ile Phe Phe Leu Ser Ile Leu Val Leu | | | |
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| Ser Phe Ile Tyr Leu Arg Pro Thr Ser Leu Tyr Ser Ser Asp Lys Asp | | | |
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| His Thr Pro Met Tyr Phe Phe Leu Phe Val Leu Ser Cys Ser Glu Thr | | | |
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| | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | |
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| Val | Cys | Leu | Asp | Ser | Arg | Leu | His | Thr | Pro | Met | Tyr | His | Phe | Val | Ser |
| | | | | | | | | 50 | | 55 | | | 60 | | |

| | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | |
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| Met | Leu | Ala | Asn | Leu | Leu | Ser | Glu | Lys | Lys | Thr | Ile | Ser | Phe | Ser | Gly |
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| Cys | Leu | Leu | Gln | Ile | Tyr | Phe | Phe | His | Ser | Leu | Gly | Ala | Thr | Glu | Cys |
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| | | | | | | | | | | | | | | | |
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| Tyr | Leu | Leu | Thr | Ala | Met | Ala | Tyr | Asp | Arg | Tyr | Leu | Ala | Ile | Cys | Arg |
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| | | | | | | | | | | | | | | | |
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| | | | | | | | | | | | | | | | |
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| Ala | Ile | Gly | Cys | Trp | Leu | Gly | Gly | Leu | Ala | Gly | Pro | Val | Val | Glu | Ile |
| | | | | | | | | 145 | | 150 | | | 155 | | 160 |

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| tat gtc ttt cat tcc tta ggg atg act gag tgc tac ctg ctg ggt gtc Tyr Val Phe His Ser Leu Gly Met Thr Glu Cys Tyr Leu Leu Gly Val 80 85 90 95 | 290 |
| atg gca ctg gat agc tac ctt atc atc tgc cac cca ctc cac tac cac Met Ala Leu Asp Ser Tyr Leu Ile Ile Cys His Pro Leu His Tyr His 100 105 110 | 338 |
| gca ctc atg agc aga cag gta cag tta cga cta gct ggg gcc agt tgg Ala Leu Met Ser Arg Gln Val Gln Leu Arg Leu Ala Gly Ala Ser Trp 115 120 125 | 386 |
| gtg gct ggc ttc tca gct gca ctt gtg cca gcc acc ctc act gcc act Val Ala Gly Phe Ser Ala Ala Leu Val Pro Ala Thr Leu Thr Ala Thr 130 135 140 | 434 |
| ctg ccc ttc tgc ttg aaa gag gtg gcc cat tac ttt tgt gac ttg gca Leu Pro Phe Cys Leu Lys Glu Val Ala His Tyr Phe Cys Asp Leu Ala 145 150 155 | 482 |
| cca cta atg cgg ttg gca tgt gtg gac aca agc tgg cat gct agg gcc Pro Leu Met Arg Leu Ala Cys Val Asp Thr Ser Trp His Ala Arg Ala 160 165 170 175 | 530 |
| cat ggc aca gtg att ggt gtg gcc act ggt tgc aac ttt gtg ctc att His Gly Thr Val Ile Gly Val Ala Thr Gly Cys Asn Phe Val Leu Ile 180 185 190 | 578 |
| ttg gga ctc tat gga ggt atc ctg aat gct gtg ctg aag cta ccc tca Leu Gly Leu Tyr Gly Gly Ile Leu Asn Ala Val Leu Lys Leu Pro Ser 195 200 205 | 626 |
| gct gcc agt agt gcc aag gcc ttc tct acc tgc tcc tcc cac gta act Ala Ala Ser Ser Ala Lys Ala Phe Ser Thr Cys Ser Ser His Val Thr 210 215 220 | 674 |
| gtg gtg gca cta ttc tat gct tct gcc ttc aca gta tat gtg ggc tca Val Val Ala Leu Phe Tyr Ala Ser Ala Phe Thr Val Tyr Val Gly Ser 225 230 235 | 722 |
| cct ggg agt cga cct gag agc aca gac aag ctt gtt gcc ttg gtt tat Pro Gly Ser Arg Pro Glu Ser Thr Asp Lys Leu Val Ala Leu Val Tyr 240 245 250 255 | 770 |
| gcc ctt att acc cct ttc ctc aat cct atc atc tat agc ctt cgc aac Ala Leu Ile Thr Pro Phe Leu Asn Pro Ile Ile Tyr Ser Leu Arg Asn 260 265 270 | 818 |
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<213> Homo sapiens

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Cys Ile Tyr Leu Leu Thr Leu Ala Gly Asn Ile Leu Ile Val Leu
 35 40 45

Arg Cys Gly Met Ser Ala Pro Gln Cys Pro Cys Cys Cys Thr Pro Cys
 50 55 60

Ser Lys Gly Val His Pro Ser His Gln Leu Tyr Ala Leu Phe Ser Tyr
 65 70 75 80

Val Phe His Ser Leu Gly Met Thr Glu Cys Tyr Leu Leu Gly Val Met
 85 90 95

Ala Leu Asp Ser Tyr Leu Ile Ile Cys His Pro Leu His Tyr His Ala
 100 105 110

Leu Met Ser Arg Gln Val Gln Leu Arg Leu Ala Gly Ala Ser Trp Val
 115 120 125

Ala Gly Phe Ser Ala Ala Leu Val Pro Ala Thr Leu Thr Ala Thr Leu
 130 135 140

Pro Phe Cys Leu Lys Glu Val Ala His Tyr Phe Cys Asp Leu Ala Pro
 145 150 155 160

Leu Met Arg Leu Ala Cys Val Asp Thr Ser Trp His Ala Arg Ala His
 165 170 175

Gly Thr Val Ile Gly Val Ala Thr Gly Cys Asn Phe Val Leu Ile Leu
 180 185 190

Gly Leu Tyr Gly Gly Ile Leu Asn Ala Val Leu Lys Leu Pro Ser Ala
 195 200 205

Ala Ser Ser Ala Lys Ala Phe Ser Thr Cys Ser Ser His Val Thr Val
 210 215 220

Val Ala Leu Phe Tyr Ala Ser Ala Phe Thr Val Tyr Val Gly Ser Pro
 225 230 235 240

Gly Ser Arg Pro Glu Ser Thr Asp Lys Leu Val Ala Leu Val Tyr Ala
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Glu Leu Leu Tyr Cys Phe Leu Cys
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Met Val Thr Glu Phe Leu Leu Leu Gly Phe Ser Ser Leu Gly Glu Ile
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48

cag ctg gcc ctc ttt gta gtt ttt ctt ttt ctg tat cta gtc att ctt
Gln Leu Ala Leu Phe Val Val Phe Leu Phe Leu Tyr Leu Val Ile Leu
20 25 30

96

agt gtc aat gtc acc att atc agt gtc atc cac ctg gat aaa agc ctc
Ser Gly Asn Val Thr Ile Ile Ser Val Ile His Leu Asp Lys Ser Leu
35 40 45

144

cac aca cca atg tac ttc ttc ctt ggc att ctc tca aca tct gag acc
His Thr Pro Met Tyr Phe Phe Leu Gly Ile Leu Ser Thr Ser Glu Thr
50 55 60

192

ttc tac acc ttt gtc att cta ccc aag atg ctc atc aat cta ctt tct
Phe Tyr Thr Phe Val Ile Leu Pro Lys Met Leu Ile Asn Leu Leu Ser
65 70 75 80

240

gtg gcc agg aca atc tcc ttc aac tgt tgt gct cttcaa atg ttc ttc
Val Ala Arg Thr Ile Ser Phe Asn Cys Cys Ala Leu Gln Met Phe Phe
85 90 95

288

ttc ctt ggt ttt gcc att acc aac tgc ctg cta ttg ggt gtg atg ggt
Phe Leu Gly Phe Ala Ile Thr Asn Cys Leu Leu Leu Gly Val Met Gly

336

| | | 16U 200 PCT FINAL.ST25 | |
|--|-----|-------------------------------|-------------|
| 100 | 105 | 110 | |
| tat gat cgc tat gct gcc att tgt cac cct ctg cat tac ccc act ctt | | | 384 |
| Tyr Asp Arg Tyr Ala Ala Ile Cys His Pro Leu His Tyr Pro Thr Leu | | | |
| 115 | 120 | 125 | |
| atg agc tgg cag gtg tgt gga aaa ctg gca gct gcc tgt gca att ggt | | | 432 |
| Met Ser Trp Gln Val Cys Gly Lys Leu Ala Ala Ala Cys Ala Ile Gly | | | |
| 130 | 135 | 140 | |
| ggc ttc ttg gcc tct ctt aca gta gta aat tta gtt ttc agc ctc cct | | | 480 |
| Gly Phe Leu Ala Ser Leu Thr Val Val Asn Leu Val Phe Ser Leu Pro | | | |
| 145 | 150 | 155 | 160 |
| ttt tgt agc gcc aac aaa gtc aat cat tac ttc tgt gac atc tca gca | | | 528 |
| Phe Cys Ser Ala Asn Lys Val Asn His Tyr Phe Cys Asp Ile Ser Ala | | | |
| 165 | 170 | 175 | |
| gtc att ctt ctg gct tgt acc aac aca gat gtt aac gaa ttt gtg ata | | | 576 |
| Val Ile Leu Leu Ala Cys Thr Asn Thr Asp Val Asn Glu Phe Val Ile | | | |
| 180 | 185 | 190 | |
| ttc att tgt gga gtt ctt gta ctt gtg gtt ccc ttt ctg ttt atc tgt | | | 624 |
| Phe Ile Cys Gly Val Leu Val Val Pro Phe Leu Phe Ile Cys | | | |
| 195 | 200 | 205 | |
| gtt tct tat ctc tgc att ctg agg act atc ctg aag att ccc tca gct | | | 672 |
| Val Ser Tyr Leu Cys Ile Leu Arg Thr Ile Leu Lys Ile Pro Ser Ala | | | |
| 210 | 215 | 220 | |
| gag ggc aga cgg aaa gcg ttt tcc acc tgc gcc tct cac ctc agt gtt | | | 720 |
| Glu Gly Arg Arg Lys Ala Phe Ser Thr Cys Ala Ser His Leu Ser Val | | | |
| 225 | 230 | 235 | 240 |
| gtt att gtt cat tat ggc tgt gct tcc ttc atc tac ctg agg cct aca | | | 768 |
| Val Ile Val His Tyr Gly Cys Ala Ser Phe Ile Tyr Leu Arg Pro Thr | | | |
| 245 | 250 | 255 | |
| gca aac tat gtg tcc aac aaa gac agg ctg gtg acg gtg aca tac acg | | | 816 |
| Ala Asn Tyr Val Ser Asn Lys Asp Arg Leu Val Thr Val Thr Tyr Thr | | | |
| 260 | 265 | 270 | |
| att gtc act cca tta cta aac ccc atg gtt tat agc ctc aga aac aag | | | 864 |
| Ile Val Thr Pro Leu Leu Asn Pro Met Val Tyr Ser Leu Arg Asn Lys | | | |
| 275 | 280 | 285 | |
| gat gtc caa ctt gct atc aga aaa gtg ttg ggc aag aaa ggt att ctt | | | 912 |
| Asp Val Gln Leu Ala Ile Arg Lys Val Leu Gly Lys Lys Gly Ile Leu | | | |
| 290 | 295 | 300 | |
| tct atc tct gaa atc ttc tac aca act gtt att ctg ccc aag atg ctt | | | 960 |
| Ser Ile Ser Glu Ile Phe Tyr Thr Val Ile Leu Pro Lys Met Leu | | | |
| 305 | 310 | 315 | 320 |
| atc aac tta ttc tct gta ttc agg aca ctc tcc ttt gtg agt tgt gcc | | | 1008 |
| Ile Asn Leu Phe Ser Val Phe Arg Thr Leu Ser Phe Val Ser Cys Ala | | | |
| 325 | 330 | 335 | |
| acc caa atg ttc ttc ctc ggt ttt gct gtc act aac tgt ctg ctt | | | 1056 |
| Thr Gln Met Phe Phe Leu Gly Phe Ala Val Thr Asn Cys Leu Leu | | | |
| 340 | 345 | 350 | |
| ctg gga gtg atg ggt tat gat cgt tat gct gcc atc tgt cag cct ttg | | | 1104 |
| Leu Gly Val Met Gly Tyr Asp Arg Tyr Ala Ala Ile Cys Gln Pro Leu | | | |
| 355 | 360 | 365 | |
| caa tac gct gtt ctc atg agc tgg aga gta tgt gga caa ctg ata gca | | | 1152 |
| Gln Tyr Ala Val Leu Met Ser Trp Arg Val Cys Gly Gln Leu Ile Ala | | | |
| 370 | 375 | 380 | |
| act tgt att att agt ggc ttc cta ata tct ctg gtg gga aca act ttt | | | 1200 |
| Thr Cys Ile Ile Ser Gly Phe Leu Ile Ser Leu Val Gly Thr Thr Phe | | | |
| 385 | 390 | 395 | 400 |
| gtc ttt agc ctc cct ttc tgt ggc tcc aac aag gtc aac cac tac ttt | | | 1248 |
| Val Phe Ser Leu Pro Phe Cys Gly Ser Asn Lys Val Asn His Tyr Phe | | | |
| 405 | 410 | 415 | |
| tgt gat att tca cca gtt atc cgt ctc gct tgt gct gac agc tac atc | | | 1296 |

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|---|-----|------|-----|---|--|------|---|--|-----|-----|-----|---|--|------|---|--|-----|-----|-----|---|--|------|---|--|-----|-----|-----|-----|---|--|------|---|--|-----|-----|--|----------|--|--|-----------|--|--|-----------|--|--|--------------------|--|--|----------|--|--|---|--|--|---|---|----|----|---|--|--|----|----|----|---|--|--|----|----|----|---|--|--|----|----|----|---|--|--|----|----|----|----|---|--|--|----|----|----|---|--|--|-----|-----|-----|---|--|--|-----|-----|-----|---|--|--|-----|-----|-----|---|--|--|-----|-----|-----|-----|---|--|--|-----|-----|-----|---|--|--|-----|-----|-----|---|--|--|-----|-----|-----|
| Cys Asp Ile Ser Pro Val Ile Arg Leu Ala Cys Ala Asp Ser Tyr Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 420 | 425 | | 430 | agt gaa ctg gtc atc ttc atc ttc ggg gtc ttg gtg ctt gtt gtg ccc | | 1344 | Ser Glu Leu Val Ile Phe Ile Phe Gly Val Leu Val Val Val Pro | | 435 | 440 | 445 | ttg ata ttt atc tgc att tcc tat ggc ttc att gtc cgc acc atc ctg | | 1392 | Leu Ile Phe Ile Cys Ile Ser Tyr Gly Phe Ile Val Arg Thr Ile Leu | | 450 | 455 | 460 | aag atc cca tca gct gaa ggc aaa caa aaa gcc ttc tcc acc tgt gct | | 1440 | Lys Ile Pro Ser Ala Glu Gly Lys Gln Lys Ala Phe Ser Thr Cys Ala | | 465 | 470 | 475 | 480 | tcc cat ctc att gta gtc att gtc cat tat ggt tga | | 1476 | Ser His Leu Ile Val Val Ile Val His Tyr Gly | | 485 | 490 | | <210> 48 | | | <211> 491 | | | <212> PRT | | | <213> Homo sapiens | | | <400> 48 | | | Met Val Thr Glu Phe Leu Leu Leu Gly Phe Ser Ser Leu Gly Glu Ile | | | 1 | 5 | 10 | 15 | Gln Leu Ala Leu Phe Val Val Phe Leu Phe Leu Tyr Leu Val Ile Leu | | | 20 | 25 | 30 | Ser Gly Asn Val Thr Ile Ile Ser Val Ile His Leu Asp Lys Ser Leu | | | 35 | 40 | 45 | His Thr Pro Met Tyr Phe Phe Leu Gly Ile Leu Ser Thr Ser Glu Thr | | | 50 | 55 | 60 | Phe Tyr Thr Phe Val Ile Leu Pro Lys Met Leu Ile Asn Leu Leu Ser | | | 65 | 70 | 75 | 80 | Val Ala Arg Thr Ile Ser Phe Asn Cys Cys Ala Leu Gln Met Phe Phe | | | 85 | 90 | 95 | Phe Leu Gly Phe Ala Ile Thr Asn Cys Leu Leu Leu Gly Val Met Gly | | | 100 | 105 | 110 | Tyr Asp Arg Tyr Ala Ala Ile Cys His Pro Leu His Tyr Pro Thr Leu | | | 115 | 120 | 125 | Met Ser Trp Gln Val Cys Gly Lys Leu Ala Ala Ala Cys Ala Ile Gly | | | 130 | 135 | 140 | Gly Phe Leu Ala Ser Leu Thr Val Val Asn Leu Val Phe Ser Leu Pro | | | 145 | 150 | 155 | 160 | Phe Cys Ser Ala Asn Lys Val Asn His Tyr Phe Cys Asp Ile Ser Ala | | | 165 | 170 | 175 | Val Ile Leu Leu Ala Cys Thr Asn Thr Asp Val Asn Glu Phe Val Ile | | | 180 | 185 | 190 | Phe Ile Cys Gly Val Leu Val Leu Val Val Pro Phe Leu Phe Ile Cys | | | 195 | 200 | 205 |
| | 430 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| agt gaa ctg gtc atc ttc atc ttc ggg gtc ttg gtg ctt gtt gtg ccc | | 1344 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ser Glu Leu Val Ile Phe Ile Phe Gly Val Leu Val Val Val Pro | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 435 | 440 | 445 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ttg ata ttt atc tgc att tcc tat ggc ttc att gtc cgc acc atc ctg | | 1392 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Ile Phe Ile Cys Ile Ser Tyr Gly Phe Ile Val Arg Thr Ile Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 450 | 455 | 460 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| aag atc cca tca gct gaa ggc aaa caa aaa gcc ttc tcc acc tgt gct | | 1440 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Lys Ile Pro Ser Ala Glu Gly Lys Gln Lys Ala Phe Ser Thr Cys Ala | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 465 | 470 | 475 | 480 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| tcc cat ctc att gta gtc att gtc cat tat ggt tga | | 1476 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ser His Leu Ile Val Val Ile Val His Tyr Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 485 | 490 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <210> 48 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <211> 491 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| <213> Homo sapiens | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Met Val Thr Glu Phe Leu Leu Leu Gly Phe Ser Ser Leu Gly Glu Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 5 | 10 | 15 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gln Leu Ala Leu Phe Val Val Phe Leu Phe Leu Tyr Leu Val Ile Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 20 | 25 | 30 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ser Gly Asn Val Thr Ile Ile Ser Val Ile His Leu Asp Lys Ser Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| His Thr Pro Met Tyr Phe Phe Leu Gly Ile Leu Ser Thr Ser Glu Thr | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 50 | 55 | 60 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Phe Tyr Thr Phe Val Ile Leu Pro Lys Met Leu Ile Asn Leu Leu Ser | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Val Ala Arg Thr Ile Ser Phe Asn Cys Cys Ala Leu Gln Met Phe Phe | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Phe Leu Gly Phe Ala Ile Thr Asn Cys Leu Leu Leu Gly Val Met Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Tyr Asp Arg Tyr Ala Ala Ile Cys His Pro Leu His Tyr Pro Thr Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Met Ser Trp Gln Val Cys Gly Lys Leu Ala Ala Ala Cys Ala Ile Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Gly Phe Leu Ala Ser Leu Thr Val Val Asn Leu Val Phe Ser Leu Pro | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Phe Cys Ser Ala Asn Lys Val Asn His Tyr Phe Cys Asp Ile Ser Ala | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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Asp Val Gln Leu Ala Ile Arg Lys Val Leu Gly Lys Lys Gly Ile Leu
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| 150 | 155 | 160 | | | | | |
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| 165 | 170 | 175 | | | | | |
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| 180 | 185 | 190 | | | | | |
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| 195 | 200 | 205 | 210 | | | | |
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| 215 | 220 | 225 | | | | | |
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| 230 | 235 | 240 | | | | | |
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16U 200 PCT FINAL.ST25
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 Tyr Ser Leu Arg Asn Lys Asp Val Lys Asp Thr Val Thr Glu Ile Leu
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 Asp Thr Lys Val Phe Ser Tyr
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Ser Gln Leu Ser Phe Val Asp Phe Cys Tyr Ser Ser Ile Ile Ala Pro
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| cca act gcc ttc ttg ttg gtg ggg att cca ggc ctg gaa cac ctg cac | 1899 |
| Pro Thr Ala Phe Leu Leu Val Gly Ile Pro Gly Leu Glu His Leu His | |
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| Gly Asn Cys Thr Leu Leu Leu Ile Ile Gln Ala Asp Ala Ala Leu His | |
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| Ley Ser Ser Ala Ley Pro Lys Met Ley Ala Ile Phe Trp Phe Arg | |
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| gat cgg gag ata aac ttc ttt gcc tgt ctg gcc cag atg ttc ttc'ctt | 2139 |
| Asp Arg Glu Ile Asn Phe Phe Ala Cys Ley Ala Gln Met Phe Phe Ley | |
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Pro Lys Met Leu Ala Ile Phe Trp Phe Arg Asp Arg Glu Ile Asn Phe
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Phe Ala Cys Leu Ala Gln Met Phe Phe Leu His Ser Phe Ser Ile Met
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Glu Ser Ala Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile
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Cys Lys Pro Leu His Tyr Thr Lys Val Leu Thr Gly Ser Leu Ile Thr
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Lys Ile Gly Met Ala Ala Val Ala Arg Ala Val Thr Leu Met Thr Pro
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Val Val Leu Asp Leu Leu Leu Val Ile Leu Ser Tyr Ile Phe Ile Leu
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Gln Ala Val Leu Leu Leu Ala Ser Gln Glu Ala His Tyr Lys Ala Phe
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Gly Thr Cys Val Ser His Ile Gly Ala Ile Leu Ala Phe Tyr Thr Thr
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768

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816

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912

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960

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16U 200 PCT FINAL.ST25

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| acc cct gag gtc ttg ctt tca gcc atg cgg gag gag ctg agc atg ggc Thr Pro Glu Val Leu Leu Ser Ala Met Arg Glu Glu Leu Ser Met Gly 95 100 105 110 | 1056 |
| cag cct cct gcc agc ctg ggc acc ctg ctc cgc atg ccc gga ctg cgc Gln Pro Pro Ala Ser Leu Gly Thr Leu Leu Arg Met Pro Gly Leu Arg 115 120 125 | 1104 |
| ttc cgg acc tgt atc tcc acg ttg tgc tgg ttc gcc ttt ggc ttc acc Phe Arg Thr Cys Ile Ser Thr Leu Cys Trp Phe Ala Phe Gly Phe Thr 130 135 140 | 1152 |
| ttc ttc ggc ctg gcc ctg gac ctg cag gcc ctg ggc agc aac atc ttc Phe Phe Gly Leu Ala Leu Asp Leu Gln Ala Leu Gly Ser Asn Ile Phe 145 150 155 | 1200 |
| ctg ctc caa atg ttc att ggt gtc gtg gac atc cca gcc aag atg ggc Leu Leu Gln Met Phe Ile Gly Val Val Asp Ile Pro Ala Lys Met Gly 160 165 170 | 1248 |
| gcc ctg ctg ctg ctg agc cac ctg ggc cgc cgc ccc acg ctg gcc gca Ala Leu Leu Leu Ser His Leu Gly Arg Arg Pro Thr Leu Ala Ala 175 180 185 190 | 1296 |
| tcc ctg ttg ctg gca ggg ctc tgc att ctg gcc aac acg ctg gtg ccc Ser Leu Leu Ala Gly Leu Cys Ile Leu Ala Asn Thr Leu Val Pro 195 200 205 | 1344 |
| cac gaa atg ggg gct ctg cgc tca gcc ttg gcc gtg ctg ggg ctg ggc His Glu Met Gly Ala Leu Arg Ser Ala Leu Ala Val Leu Gly Leu Gly 210 215 220 | 1392 |
| ggg gtg ggg gct gcc ttc acc tgc atc acc atc tac agc agc gag ctc Gly Val Gly Ala Ala Phe Thr Cys Ile Thr Ile Tyr Ser Ser Glu Leu 225 230 235 | 1440 |
| ttc ccc act gtg ctc agg atg acg gca gtg ggc ttg ggc cag atg gca Phe Pro Thr Val Leu Arg Met Thr Ala Val Gly Leu Gly Gln Met Ala 240 245 250 | 1488 |
| gcc cgt gga gga gcc atc ctg ggg cct ctg gtc cgg ctg ctg ggt gtc Ala Arg Gly Gly Ala Ile Leu Gly Pro Leu Val Arg Leu Leu Gly Val 255 260 265 270 | 1536 |
| cat ggc ccc tgg ctg ccc ttg ctg gtg tat ggg acg gtg cca gtg ctg His Gly Pro Trp Leu Pro Leu Leu Val Tyr Gly Thr Val Pro Val Leu 275 280 285 | 1584 |
| agt ggc ctg gcc gca ctg ctt ctg ccc gag acc cag agc ttg ccg ctg Ser Gly Leu Ala Ala Leu Leu Pro Glu Thr Gln Ser Leu Pro Leu 290 295 300 | 1632 |
| ccc gac acc atc caa gat gtg cag aac cag gca gta aag aag gca aca Pro Asp Thr Ile Gln Asp Val Gln Asn Gln Ala Val Lys Lys Ala Thr 305 310 315 | 1680 |
| cat ggc acg ctg ggg aac tct gtc cta aaa tcc aca cag ttt His Gly Thr Leu Gly Asn Ser Val Leu Lys Ser Thr Gln Phe 320 325 330 | 1722 |
| tagcctcctg gggAACCTGC gatggggacgg tcagaggaag agacttcttc tttctctgg agaaggcagg aggaaaagcaa agacccat ttccagaggc ccagaggctg ccctctgagg tccccactct ccccccaggc tgcccccca ggtgagccct gcccctctca cagtccaaagg ggcccccttc aatactgaag gggaaaagga cagtttgatt ggcaggaggt gacccagtgc accatcaccc tgccctgccc tcgtggcttc ggagagcaga ggggtcaggc ccagggaaac gagctggct tgccaaacctt ctgcttgcact ccgcactgccc acttgtcccc ccacacccgt ccacacctgccc agagctcaga gctaaccacc atccatggtc aagaccccttc ctagctccac acaaggcagta gagtctcage tccacagctt tacccagaag ccctgtaaac ctggcccttg | 1782 1842 1902 1962 2022 2082 2142 2202 |

16U 200 PCT FINAL.ST25

gccccctccc atgtccctcc aggcctcage cacctgcccgg ccacatccctc tgccctgctgt 2262
 ccccttccca ccctcatccc tgaccgactc cacttaaccc ccaaaccag ccccccctcc 2322
 aggggtccag ggccagccctg agatgcccgt gaaactccta cccacagtta cagccacaag 2382
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 <213> Homo sapiens

<400> 79

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 20 25 30

Gly Val Arg Asp Trp Thr Leu Leu Gln Leu Val Val Ser Val Pro Phe
 35 40 45

Phe Leu Cys Phe Leu Tyr Ser Trp Trp Leu Ala Glu Ser Ala Arg Trp
 50 55 60

Leu Leu Thr Thr Gly Arg Leu Asp Trp Gly Leu Gln Glu Leu Trp Arg
 65 70 75 80

Val Ala Ala Ile Asn Gly Lys Gly Ala Val Gln Asp Thr Leu Thr Pro
 85 90 95

Glu Val Leu Leu Ser Ala Met Arg Glu Glu Leu Ser Met Gly Gln Pro
 100 105 110

Pro Ala Ser Leu Gly Thr Leu Leu Arg Met Pro Gly Leu Arg Phe Arg
 115 120 125

Thr Cys Ile Ser Thr Leu Cys Trp Phe Ala Phe Gly Phe Thr Phe Phe
 130 135 140

Gly Leu Ala Leu Asp Leu Gln Ala Leu Gly Ser Asn Ile Phe Leu Leu
 145 150 155 160

Gln Met Phe Ile Gly Val Val Asp Ile Pro Ala Lys Met Gly Ala Leu
 165 170 175

Leu Leu Leu Ser His Leu Gly Arg Arg Pro Thr Leu Ala Ala Ser Leu
 180 185 190

Leu Leu Ala Gly Leu Cys Ile Leu Ala Asn Thr Leu Val Pro His Glu
 195 200 205

Met Gly Ala Leu Arg Ser Ala Leu Ala Val Leu Gly Leu Gly Gly Val
 210 215 220

Gly Ala Ala Phe Thr Cys Ile Thr Ile Tyr Ser Ser Glu Leu Phe Pro
 225 230 235 240

16U 200 PCT FINAL.ST25

Thr Val Leu Arg Met Thr Ala Val Gly Leu Gly Gln Met Ala Ala Arg
 245 250 255

Gly Gly Ala Ile Leu Gly Pro Leu Val Arg Leu Leu Gly Val His Gly
 260 265 270

Pro Trp Leu Pro Leu Leu Val Tyr Gly Thr Val Pro Val Leu Ser Gly
 275 280 285

Leu Ala Ala Leu Leu Leu Pro Glu Thr Gln Ser Leu Pro Leu Pro Asp
 290 295 300

Thr Ile Gln Asp Val Gln Asn Gln Ala Val Lys Lys Ala Thr His Gly
 305 310 315 320

Thr Leu Gly Asn Ser Val Leu Lys Ser Thr Gln Phe
 325 330

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<400> 80
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ggc tcc cag gat gcc ctg gcc ccc ttg cct cca cct gct ccc cag aat 99
 Gly Ser Gln Asp Ala Leu Ala Pro Leu Pro Pro Ala Pro Gln Asn
 15 20 25 30

ccc tcc acc cac tct tgg gac cct ttg ttt gga tct ctg cct tgg ggc 147
 Pro Ser Thr His Ser Trp Asp Pro Leu Cys Gly Ser Leu Pro Trp Gly
 35 40 45

ctc agc tgt ctt ctg gct ctg cag cat gtc ttg gtc atg gct tct ctg 195
 Leu Ser Cys Leu Leu Ala Leu Gln His Val Leu Val Met Ala Ser Leu
 50 55 60

ctc tgt gtc tcc cac ctg ctc ctg ctt tgc agt ctc tcc cca gga gga 243
 Leu Cys Val Ser His Leu Leu Leu Cys Ser Leu Ser Pro Gly Gly
 65 70 75

ctc tct tac tcc cct tct cag ctc ctg gcc tcc agc ttc ttt tca tgt 291
 Leu Ser Tyr Ser Pro Ser Gln Leu Ala Ser Ser Phe Phe Ser Cys
 80 85 90

ggt atg tct acc atc ctg caa act tgg atg ggc agc agg ctg cct ctt 339
 Gly Met Ser Thr Ile Leu Gln Thr Trp Met Gly Ser Arg Leu Pro Leu
 95 100 105 110

gtc cag gct cca tcc tta gag ttc ctt atc cct gct ctg gtg ctg acc 387
 Val Gln Ala Pro Ser Leu Glu Phe Leu Ile Pro Ala Leu Val Leu Thr
 115 120 125

agc cag aag cta ccc cgg gcc atc cag aca cct gga aac tcc tcc ctc 435
 Ser Gln Lys Leu Pro Arg Ala Ile Gln Thr Pro Gly Asn Ser Ser Leu
 130 135 140

atg ctg cac ctt tgt agg gga cct agc tgc cat ggc ctg ggg cac tgg 483
 Met Leu His Leu Cys Arg Gly Pro Ser Cys His Gly Leu Gly His Trp
 145 150 155

aac act tct ctc cag gag gtg tcc ggg gca gtg gta gta tct ggg ctg 531
 Asn Thr Ser Leu Gln Glu Val Ser Gly Ala Val Val Val Ser Gly Leu

| 160 | 165 | 160 200 PCT FINAL.ST25 170 | |
|---|-----|-------------------------------|------|
| Ctg cag ggc atg atg ggg ctg ctg ggg agt ccc ggc cac gtg ttc ccc | | | 579 |
| Leu Gln Gly Met Met Gly Leu Leu Gly Ser Pro Gly His Val Phe Pro | | | |
| 175 180 185 190 | | | |
| cac tgt ggg ccc ctg gtg ctg gct ccc agc ctg gtt gtg gca ggg ctc | | | 627 |
| His Cys Gly Pro Leu Val Leu Ala Pro Ser Leu Val Val Ala Gly Leu | | | |
| 195 200 205 | | | |
| tct gcc cac agg gag gta gcc cag ttc tgc ttc aca cac tgg ggg ttg | | | 675 |
| Ser Ala His Arg Glu Val Ala Gln Phe Cys Phe Thr His Trp Gly Leu | | | |
| 210 215 220 | | | |
| gcc ttg ctg tac gtg agt cct gag agg cgt ggg atg gtg ccc agt ggg | | | 723 |
| Ala Leu Leu Tyr Val Ser Pro Glu Arg Arg Gly Met Val Pro Ser Gly | | | |
| 225 230 235 | | | |
| ggg gta tgg ggg gac taggggaggc cagaactgct ggtccatca gattcagcag | | | 778 |
| Gly Val Trp Gly Asp | | | |
| 240 | | | |
| cgactggaat agggacatat ttttatattt gaatccaaga cttttcccttg attcatctgg | | | 838 |
| tctccttcaa tttcacactg tttctgctg tcccccaagg tcacttccta ttccttccat | | | 898 |
| gggagttcc ttctctggta tcaccccccg ctcttatgat attctgccc a tcccaccc | | | 958 |
| ctttcccatc ctcaggata cccactgcct cttgctccca aagccttctg tctcttaggg | | | 1018 |
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| cctggaggcg agcttcaacg tcatcaactc acactccctc ccctgtcttc cggctccccc | | | 1138 |
| cggatgtgtt gggctggc agggcagtag aggtcagaag ggctggctg gagtgcac | | | 1198 |
| tccatccccct acctttggc ttctgtctac ccctgcaagg ctggctcaga aggttctggg | | | 1258 |
| ggaggagttc ttttctca gtcggccctc aggtgtctgat ccctgtggc ttttctgg | | | 1318 |
| ttgtttctgc ctttgtggg ttcagtgtta tcccccaagg actgtctgcc cccaccaagg | | | 1378 |
| caccatggat ttggctgcct caccctggc agtggaaattt gcctttgtcg acgcccagag | | | 1438 |
| ctctggctgc aggcatctcc atggccttgg cagcctccac cagttccctg ggctgtatg | | | 1498 |
| ccctgtgtgg cggcgtctg catttgcctc cccacccctc acatgcctgc agtcgaggc | | | 1558 |
| tgagcctggc gggctggc agtggctgg cggggctgt gggaaagcccc atgggcactg | | | 1618 |
| catccagctt ccccaacgtg ggcaaaagtgg gtcttatcca ggtacgtgg cctggatgg | | | 1678 |
| gagtggggta ggtggagct agagggaaag aagaaggaca ggaacttaca ccgattgatt | | | 1738 |
| gccagggtgt cctagcacct cacaatcaact atcttacttg gggagggtgcc taagattaga | | | 1798 |
| ctttgggcta agagagtggg gaagtgaaca aatcaccacg gaactcctgt gcatgaggca | | | 1858 |
| ctgtatcaag gctaggc aaagaccagtc acataaaatgtt ctgtctctt gggacttca | | | 1918 |
| tagagggaga ggcagacagt tgaaggaaaa aagtatctt ttaaaaaaagt gggccaggca | | | 1978 |
| ttggtggctca cactgttaat cctagcacgt gggggaggctg agggcaggcag atcactttagg | | | 2038 |
| cttagaaatc aagaccagcc tggccaacat ggtgaaaccc tttttttttttt aaaaatacaa | | | 2098 |
| aaatttagctg ggcattgggtgt tttttttttttt tttttttttttt aaaaatacaa | | | 2158 |
| gagaatcgct tgagcctggg aggcagaggt tttttttttttt tttttttttttt aaaaatacaa | | | 2218 |
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<210> 81
<211> 243
<212> PRT
<213> Homo sapiens
<400> 81

16U 200 PCT FINAL.ST25

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Gln Asp Ala Leu Ala Pro Leu Pro Pro Ala Pro Gln Asn Pro Ser
 20 25 30

Thr His Ser Trp Asp Pro Leu Cys Gly Ser Leu Pro Trp Gly Leu Ser
 35 40 45

Cys Leu Leu Ala Leu Gln His Val Leu Val Met Ala Ser Leu Leu Cys
 50 55 60

Val Ser His Leu Leu Leu Cys Ser Leu Ser Pro Gly Gly Leu Ser
 65 70 75 80

Tyr Ser Pro Ser Gln Leu Leu Ala Ser Ser Phe Phe Ser Cys Gly Met
 85 90 95

Ser Thr Ile Leu Gln Thr Trp Met Gly Ser Arg Leu Pro Leu Val Gln
 100 105 110

Ala Pro Ser Leu Glu Phe Leu Ile Pro Ala Leu Val Leu Thr Ser Gln
 115 120 125

Lys Leu Pro Arg Ala Ile Gln Thr Pro Gly Asn Ser Ser Leu Met Leu
 130 135 140

His Leu Cys Arg Gly Pro Ser Cys His Gly Leu Gly His Trp Asn Thr
 145 150 155 160

Ser Leu Gln Glu Val Ser Gly Ala Val Val Val Ser Gly Leu Leu Gln
 165 170 175

Gly Met Met Gly Leu Leu Gly Ser Pro Gly His Val Phe Pro His Cys
 180 185 190

Gly Pro Leu Val Leu Ala Pro Ser Leu Val Val Ala Gly Leu Ser Ala
 195 200 205

His Arg Glu Val Ala Gln Phe Cys Phe Thr His Trp Gly Leu Ala Leu
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Leu Tyr Val Ser Pro Glu Arg Arg Gly Met Val Pro Ser Gly Gly Val
 225 230 235 240

Trp Gly Asp

<210> 82
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<213> Homo sapiens

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<222> (99)..(1508)
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ttgtaatttataatggatccatcaacatccttcaattacaatgtatcgatagaaggagaaa 116

160 200 PCT FINAL.ST25
Met Asp Arg Gly Glu Lys
1 5

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| ata cag ctc aag aga gtg ttt gga tat tgg tgg ggc aca agt ttt ttg Ile Gln Leu Lys Arg Val Phe Gly Tyr Trp Trp Gly Thr Ser Phe Leu 10 15 20 | 164 |
| cgt att aat atc att ggt gca gga att ttt gtg tcc ccc aaa ggt gtg Leu Ile Asn Ile Ile Gly Ala Gly Ile Phe Val Ser Pro Lys Gly Val 25 30 35 | 212 |
| ttg gca tac tct tgc atg aac gtg gga gtc tcc ctg tgc gtt tgg gct Leu Ala Tyr Ser Cys Met Asn Val Gly Val Ser Leu Cys Val Trp Ala 40 45 50 | 260 |
| ggc tgt gcc ata ctg gcc atg aca tca act ctt tgc tct gca gag ata Gly Cys Ala Ile Leu Ala Met Thr Ser Thr Leu Cys Ser Ala Glu Ile 55 60 65 70 | 308 |
| agt ata agc ttc cca tgc agt gga gct caa tac tat ttt ctc aag aga Ser Ile Ser Phe Pro Cys Ser Gly Ala Gln Tyr Tyr Phe Leu Lys Arg 75 80 85 | 356 |
| tac ttt ggc tcc acg gtt gct ttt ttg aat ctc tgg aca tcc ttg ttt Tyr Phe Gly Ser Thr Val Ala Phe Leu Asn Leu Trp Thr Ser Leu Phe 90 95 100 | 404 |
| ctg ggg tca ggg gta gtt gct ggc caa gct ctg ctc ctt gct gag tac Leu Gly Ser Gly Val Val Ala Gly Gln Ala Leu Leu Ala Glu Tyr 105 110 115 | 452 |
| agc atc cag cct ttt ccc agc tgc tct gtc cca aag ctg cct aag Ser Ile Gln Pro Phe Pro Ser Cys Ser Val Pro Lys Leu Pro Lys 120 125 130 | 500 |
| aaa tgt ctg gca ttg gcc atg ttg tgg att gta gga att ctg act tct Lys Cys Leu Ala Leu Ala Met Leu Trp Ile Val Gly Ile Leu Thr Ser 135 140 145 150 | 548 |
| cgt ggt gtg aaa gaa gtg act ttg ctt cag ata gct agc tca gtg ctg Arg Gly Val Lys Glu Val Thr Trp Leu Gln Ile Ala Ser Ser Val Leu 155 160 165 | 596 |
| aaa gtg tcc ata ctt agc ttc att tcc cta act gga gta gtg ttc ctg Lys Val Ser Ile Leu Ser Phe Ile Ser Leu Thr Gly Val Val Phe Leu 170 175 180 | 644 |
| ata aga ggg aaa aag gag aat gta gaa cga ttt cag aat gct ttt gat Ile Arg Gly Lys Lys Glu Asn Val Glu Arg Phe Gln Asn Ala Phe Asp 185 190 195 | 692 |
| gct gaa ctt cca gat atc tct cac ctt ata caa gcc atc ttc caa gga Ala Glu Leu Pro Asp Ile Ser His Leu Ile Gln Ala Ile Phe Gln Gly 200 205 210 | 740 |
| tat ttt gca tat tca ggc ggg gca tgc ttt aca ctt ata gca ggg gag Tyr Phe Ala Tyr Ser Gly Gly Ala Cys Phe Thr Leu Ile Ala Gly Glu 215 220 225 230 | 788 |
| ctg aag aag ccc aga aca aca att ccc aaa tgc ata ttt act gcg tta Leu Lys Pro Arg Thr Thr Ile Pro Lys Cys Ile Phe Thr Ala Leu 235 240 245 | 836 |
| cct ctg gtg act gta gtt tat tta ctg gtt aac att tcc tat ctg act Pro Leu Val Thr Val Val Tyr Leu Leu Val Asn Ile Ser Tyr Leu Thr 250 255 260 | 884 |
| gtt ctg aca ccc agg gaa att ctc tct tca gat gct gta gct atc aca Val Leu Thr Pro Arg Glu Ile Leu Ser Ser Asp Ala Val Ala Ile Thr 265 270 275 | 932 |
| tgg gct gat cga gct ttt ccc tca tta gca tgg att atg cct ttt gct Trp Ala Asp Arg Ala Phe Pro Ser Leu Ala Trp Ile Met Pro Phe Ala 280 285 290 | 980 |
| att tct acc tca tta ttt agc aac ctt ctg att tct ata ttt aaa tca Ile Ser Thr Ser Leu Phe Ser Asn Leu Leu Ile Ser Ile Phe Lys Ser 295 300 305 310 | 1028 |

<210> 83
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<212> PRT
<213> *Homo sapiens*

<400> 83

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Trp Gly Thr Ser Phe Leu Leu Ile Asn Ile Ile Gly Ala Gly Ile Phe
20 25 30

Val Ser Pro Lys Gly Val Leu Ala Tyr Ser Cys Met Asn Val Gly Val
35 40 45

Ser Leu Cys Val Trp Ala Gly Cys Ala Ile Leu Ala Met Thr Ser..Thr
50 55 60

Leu Cys Ser Ala Glu Ile Ser Ile Ser Phe Pro Cys Ser Gly Ala Gln
65 70 75 80

16U 200 PCT FINAL.ST25

Tyr Tyr Phe Leu Lys Arg Tyr Phe Gly Ser Thr Val Ala Phe Leu Asn
 85 90 95

Leu Trp Thr Ser Leu Phe Leu Gly Ser Gly Val Val Ala Gly Gln Ala
 100 105 110

Leu Leu Leu Ala Glu Tyr Ser Ile Gln Pro Phe Phe Pro Ser Cys Ser
 115 120 125

Val Pro Lys Leu Pro Lys Lys Cys Leu Ala Leu Ala Met Leu Trp Ile
 130 135 140

Val Gly Ile Leu Thr Ser Arg Gly Val Lys Glu Val Thr Trp Leu Gln
 145 150 155 160

Ile Ala Ser Ser Val Leu Lys Val Ser Ile Leu Ser Phe Ile Ser Leu
 165 170 175

Thr Gly Val Val Phe Leu Ile Arg Gly Lys Lys Glu Asn Val Glu Arg
 180 185 190

Phe Gln Asn Ala Phe Asp Ala Glu Leu Pro Asp Ile Ser His Leu Ile
 195 200 205

Gln Ala Ile Phe Gln Gly Tyr Phe Ala Tyr Ser Gly Gly Ala Cys Phe
 210 215 220

Thr Leu Ile Ala Gly Glu Leu Lys Lys Pro Arg Thr Thr Ile Pro Lys
 225 230 235 240

Cys Ile Phe Thr Ala Leu Pro Leu Val Thr Val Val Tyr Leu Leu Val
 245 250 255

Asn Ile Ser Tyr Leu Thr Val Leu Thr Pro Arg Glu Ile Leu Ser Ser
 260 265 270

Asp Ala Val Ala Ile Thr Trp Ala Asp Arg Ala Phe Pro Ser Leu Ala
 275 280 285

Trp Ile Met Pro Phe Ala Ile Ser Thr Ser Leu Phe Ser Asn Leu Leu
 290 295 300

Ile Ser Ile Phe Lys Ser Ser Arg Pro Ile Tyr Leu Ala Ser Gln Glu
 305 310 315 320

Gly Gln Leu Pro Leu Leu Phe Asn Thr Leu Asn Ser His Ser Ser Pro
 325 330 335

Phe Thr Ala Val Leu Leu Leu Val Thr Leu Gly Ser Leu Ala Ile Ile
 340 345 350

Leu Thr Ser Leu Ile Asp Leu Ile Asn Tyr Ile Phe Phe Thr Gly Ser
 355 360 365

Leu Trp Ser Ile Leu Leu Met Ile Gly Ile Leu Arg Arg Arg Tyr Gln
 370 375 380

Glu Pro Asn Leu Ser Ile Pro Tyr Lys Val Phe Leu Ser Phe Pro Leu
 385 390 395 400

16U 200 PCT FINAL.ST25

Ala Thr Ile Val Ile Asp Val Gly Leu Val Val Ile Pro Leu Val Lys
 405 410 415

Ser Pro Asn Val His Tyr Val Tyr Val Leu Leu Leu Val Ser Gly
 420 425 430

Leu Leu Phe Tyr Ile Pro Leu Ile His Phe Lys Ile Arg Leu Ala Trp
 435 440 445

Phe Glu Lys Met Thr Cys Tyr Leu Gln Leu Leu Phe Asn Ile Cys Leu
 450 455 460

Pro Asp Val Ser Glu Glu
 465 470

<210> 84
 <211> 1046
 <212> DNA
 <213> Homo sapiens

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 <222> (319)..(852)
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 tgaagtcaac ttttgagatc ttcaacttacat acacgttggt gtctgaagat tcacacgagt 180
 gcctctggta atcatttct tcagggaaatc acagtctctc ctctcagcaa agcatccact 240
 gtactgaact ttgc当地gg aaacatcttc ttccctgagac ctc当地gaaa gaaactctct 300
 ggtgtcatac ttccaaat atg gag gtg aag aac ttt gca gtt tgg gat tat 351
 Met Glu Val Lys Asn Phe Ala Val Trp Asp Tyr
 1 5 10
 gtt gta ttt gca gcc ctc ttt ttc att tcc tct gga att ggg gtg ttc 399
 Val Val Phe Ala Ala Leu Phe Phe Ile Ser Ser Gly Ile Gly Val Phe
 15 20 25
 ttt gcc att aag gag aga aaa aag gca act tcc cga gag ttc ctg gtt 447
 Phe Ala Ile Lys Glu Arg Lys Lys Ala Thr Ser Arg Glu Phe Leu Val
 30 35 40
 ggg gga agg caa atg agc ttt ggc cct gtc ggc ttg tct ctg aca gcc 495
 Gly Gly Arg Gln Met Ser Phe Gly Pro Val Gly Leu Ser Leu Thr Ala
 45 50 55
 agc ttc atg tca gct gtc acg gtc ctg ggg acc cct tct gaa gtc tac 543
 Ser Phe Met Ser Ala Val Thr Val Leu Gly Thr Pro Ser Glu Val Tyr
 60 65 70 75
 cgc ttt ggg gca tcc ttc cta gtc ttc att gct tac cta ttt gtc 591
 Arg Phe Gly Ala Ser Phe Leu Val Phe Phe Ile Ala Tyr Leu Phe Val
 80 85 90
 atc ctc tta aca tca gag ctc ttt ctc cct gtg ttc tac aga tct ggt 639
 Ile Leu Leu Thr Ser Glu Leu Phe Leu Pro Val Phe Tyr Arg Ser Gly
 95 100 105
 atc acc agc act tat gag tac tta caa cta cga ttc aac aaa cca gtt 687
 Ile Thr Ser Thr Tyr Glu Tyr Leu Gln Leu Arg Phe Asn Lys Pro Val
 110 115 120
 cgc tat gct gcc acg gtc atc tac att gta cag acg att ctc tac aca 735
 Arg Tyr Ala Ala Thr Val Ile Tyr Ile Val Gln Thr Ile Leu Tyr Thr
 125 130 135

160 200 PCT FINAL.ST25
 gga gtg gtg gtg tat gct cct gcc ctg gca ctc aat caa gtg act ggg 783
 Gly Val Val Val Tyr Ala Pro Ala Leu Ala Leu Asn Gln Val Thr Gly
 140 145 150 155

ttt gat ctc tgg ggc tct gtg ttt gca aca gga att gtt tgc aca ttc 831
 Phe Asp Leu Trp Gly Ser Val Phe Ala Thr Gly Ile Val Cys Thr Phe
 160 165 170

tac tgt acc ctc gta tgt atc tagctgtgaa gaagtattta acactacctc 882
 Tyr Cys Thr Leu Val Cys Ile
 175

ctaataatggg ataaggggcaa atctccagca ataggcatct aattatacgca gaattcgtaa 942
 ttccaaaatt aaggcagaagt atgtcggctt atctgtcaca gtttcctgag gaaggtgctg 1002
 ttgttaaca ttctttcat taccaacctt taggagaatt taat 1046

<210> 85
<211> 178
<212> PRT
<213> Homo sapiens

<400> 85

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 20 25 30

Arg Lys Lys Ala Thr Ser Arg Glu Phe Leu Val Gly Gly Arg Gln Met
 35 40 45

Ser Phe Gly Pro Val Gly Leu Ser Leu Thr Ala Ser Phe Met Ser Ala
 50 55 60

Val Thr Val Leu Gly Thr Pro Ser Glu Val Tyr Arg Phe Gly Ala Ser
 65 70 75 80

Phe Leu Val Phe Phe Ile Ala Tyr Leu Phe Val Ile Leu Leu Thr Ser
 85 90 95

Glu Leu Phe Leu Pro Val Phe Tyr Arg Ser Gly Ile Thr Ser Thr Tyr
 100 105 110

Glu Tyr Leu Gln Leu Arg Phe Asn Lys Pro Val Arg Tyr Ala Ala Thr
 115 120 125

Val Ile Tyr Ile Val Gln Thr Ile Leu Tyr Thr Gly Val Val Val Tyr
 130 135 140

Ala Pro Ala Leu Ala Leu Asn Gln Val Thr Gly Phe Asp Leu Trp Gly
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Ser Val Phe Ala Thr Gly Ile Val Cys Thr Phe Tyr Cys Thr Leu Val
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Cys Ile

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16U 200 PCT FINAL.ST25

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| ggcgctccg cccagtcgc tccccggccc accgaagcgc ggatcgcgca gcctggggcc | 180 | |
| cgggaagggg ccactgcgc gggacgcggc tcggcggttg cgccccgggg gcatgtccgc | 240 | |
| gcgcgtaccgc cagggtcgca gtggtcccg cgaggccctg gcaaccacca ttctactttt | 300 | |
| tgtgtctatg agtttacta ccctaaggac ctcacatggc gagtaaccca tggccaggt | 360 | |
| agcggtctat gccaaccttg a atg cca tca gga agt cac tgg aca gca aac | 411 | |
| Met Pro Ser Gly Ser His Trp Thr Ala Asn | | |
| 1 5 10 | | |
| tct tcc aag atc ata act tgg ctg ttg gag caa cct gga aaa gaa gaa | 459 | |
| Ser Ser Lys Ile Ile Thr Trp Leu Leu Glu Gln Pro Gly Lys Glu Glu | | |
| 15 20 25 | | |
| aaa aga aaa acc atg gca aaa gta aat aga gct cgg tct acc tcc cct | 507 | |
| Lys Arg Lys Thr Met Ala Lys Val Asn Arg Ala Arg Ser Thr Ser Pro | | |
| 30 35 40 | | |
| cca gat gga ggc tgg ggc tgg atg att gtg gct ggc tgt ttc ctt gtt | 555 | |
| Pro Asp Gly Gly Trp Gly Trp Met Ile Val Ala Gly Cys Phe Leu Val | | |
| 45 50 55 | | |
| acc atc tgc aca cgg gca gtc aca aga tgt atc tca att ttt ttt gtg | 603 | |
| Thr Ile Cys Thr Arg Ala Val Thr Arg Cys Ile Ser Ile Phe Phe Val | | |
| 60 65 70 | | |
| gag ttc cag aca tac ttc act cag gat tac gca caa acg gca tgg atc | 651 | |
| Glu Phe Gln Thr Tyr Phe Thr Gln Asp Tyr Ala Gln Thr Ala Trp Ile | | |
| 75 80 85 90 | | |
| cat tcc att gta gat tgt gtg acc atg ctc tgt gct cca ctt ggg agt | 699 | |
| His Ser Ile Val Asp Cys Val Thr Met Leu Cys Ala Pro Leu Gly Ser | | |
| 95 100 105 | | |
| gtt gtc agt aac cat tta tcc tgt caa gtg gga atc atg ctg ggt ggc | 747 | |
| Val Val Ser Asn His Leu Ser Cys Gln Val Gly Ile Met Leu Gly Gly | | |
| 110 115 120 | | |
| ttg ctt gca tct act gga ctc atc ctg agc tca ttt gcc acg agt ctg | 795 | |
| Leu Leu Ala Ser Thr Gly Leu Ile Leu Ser Ser Phe Ala Thr Ser Leu | | |
| 125 130 135 | | |
| aag cat ctc tac ctc act ctg gga gtt ctt aca ggt ctt gga ttt gca | 843 | |
| Lys His Leu Tyr Leu Thr Leu Gly Val Leu Thr Gly Leu Gly Phe Ala | | |
| 140 145 150 | | |
| ctt tgt tac tct cca gct att gcc atg gtt ggc aag tac ttc agc aga | 891 | |
| Leu Cys Tyr Ser Pro Ala Ile Ala Met Val Gly Lys Tyr Phe Ser Arg | | |
| 155 160 165 170 | | |
| cgg aaa gcc ctt gct tat ggt atc gcc atg tca gga agt ggc att ggc | 939 | |
| Arg Lys Ala Leu Ala Tyr Gly Ile Ala Met Ser Gly Ser Gly Ile Gly | | |
| 175 180 185 | | |
| acc ttc atc ctg gct cct gtg gtt cag ctc ctt att gaa cag ttt tcc | 987 | |
| Thr Phe Ile Leu Ala Pro Val Val Gln Leu Leu Ile Glu Gln Phe Ser | | |
| 190 195 200 | | |
| tgg cgg gga gcc tta ctc att ctt ggg ggc ttt gtc ttg aat ctc tgt | 1035 | |
| Trp Arg Gly Ala Leu Leu Ile Leu Gly Gly Phe Val Leu Asn Leu Cys | | |
| 205 210 215 | | |
| gta tgt ggt gcc ttg atg agg cca att act ctt aaa gag gac cac aca | 1083 | |
| Val Cys Gly Ala Leu Met Arg Pro Ile Thr Leu Lys Glu Asp His Thr | | |
| 220 225 230 | | |
| act cca gag cag aac cat gtg tgt aga act cag aaa gaa gac att aag | 1131 | |

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| | |
|---|------|
| Thr Pro Glu Gln Asn His Val Cys Arg Thr Gln Lys Glu Asp Ile Lys | |
| 235 240 245 250 | |
| cgg gtg tct ccc tat tca tct ttg acc aaa gaa tgg gca cag act tgc | 1179 |
| Arg Val Ser Pro Tyr Ser Ser Leu Thr Lys Glu Trp Ala Gln Thr Cys | |
| 255 260 265 | |
| cgc tgt tgc tgt ttg cag caa gag tac agt ttt tta ctc atg tca gac | 1227 |
| Leu Cys Cys Leu Gln Gln Glu Tyr Ser Phe Leu Leu Met Ser Asp | |
| 270 275 280 | |
| ttt gtt gtg tta gcc gtc tcc gtt ctg ttt atg gct tat ggc tgc agc | 1275 |
| Phe Val Val Leu Ala Val Ser Val Leu Phe Met Ala Tyr Gly Cys Ser | |
| 285 290 295 | |
| cct ctc ttt gtg tac ttg gtg cct tat gct ttg agt gtt gga gtg agt | 1323 |
| Pro Leu Phe Val Tyr Leu Val Pro Tyr Ala Leu Ser Val Gly Val Ser | |
| 300 305 310 | |
| cat cag caa gct gct ttt ctt atg tcc ata ctt gga gtg att gac att | 1371 |
| His Gln Gln Ala Ala Phe Leu Met Ser Ile Leu Gly Val Ile Asp Ile | |
| 315 320 325 330 | |
| att ggc aat atc aca ttt gga tgg ctg acc gac aga agg tgt ctg aag | 1419 |
| Ile Gly Asn Ile Thr Phe Gly Trp Leu Thr Asp Arg Arg Cys Leu Lys | |
| 335 340 345 | |
| aat tac cag tat gtt tgc tac ctc ttt gcc gtg gga atg gat ggg ctc | 1467 |
| Asn Tyr Gln Tyr Val Cys Tyr Leu Phe Ala Val Gly Met Asp Gly Leu | |
| 350 355 360 | |
| tgc tat ctc tgc ctc cca atg ctt caa agt ctc cct ctg ctc gtg cct | 1515 |
| Cys Tyr Leu Cys Leu Pro Met Leu Gln Ser Leu Pro Leu Leu Val Pro | |
| 365 370 375 | |
| ttc tct tgt acc ttt ggc tac ttt gat ggt gcc tat gtg act ttg atc | 1563 |
| Phe Ser Cys Thr Phe Gly Tyr Phe Asp Gly Ala Tyr Val Thr Leu Ile | |
| 380 385 390 | |
| cca gta gtg acc aca gag ata gtg ggg acc acc tct ttg tca tca gcg | 1611 |
| Pro Val Val Thr Thr Glu Ile Val Gly Thr Ser Leu Ser Ser Ala | |
| 395 400 405 410 | |
| ctt ggt gtg gta tac ttc ctt cac gca gtg cca tac ttg gtg agc cca | 1659 |
| Leu Gly Val Val Tyr Phe Leu His Ala Val Pro Tyr Leu Val Ser Pro | |
| 415 420 425 | |
| ccc atc gca gga cgg ctg gta gat acc acc ggc agc tac act gca gca | 1707 |
| Pro Ile Ala Gly Arg Leu Val Asp Thr Thr Gly Ser Tyr Thr Ala Ala | |
| 430 435 440 | |
| ttc ctc ctc tgt gga ttt tca atg ata ttt agt tct gtg ttg ctt ggc | 1755 |
| Phe Leu Leu Cys Gly Phe Ser Met Ile Phe Ser Ser Val Leu Leu Gly | |
| 445 450 455 | |
| ttt gct aga ctt ata aag aga atg aga aaa acc cag ttg cag ttc att | 1803 |
| Phe Ala Arg Leu Ile Lys Arg Met Arg Lys Thr Gln Leu Gln Phe Ile | |
| 460 465 470 | |
| gcc aaa gaa tct gat cct aag ctg cag cta tgg acc aat gga tca gtg | 1851 |
| -Ala Lys Glu Ser Asp Pro Lys Leu Gln Leu Phe Thr Asn Gly Ser Val | |
| 475 480 485 490 | |
| gct tat tct gtg gca aga gaa ttg gat cag aaa cat ggg gag cct gtg | 1899 |
| Ala Tyr Ser Val Ala Arg Glu Leu Asp Gln Lys His Gly Glu Pro Val | |
| 495 500 505 | |
| gct aca gca gtg cct ggc tac agc ctc aca tgaccaaagg ccttgagccc | 1949 |
| Ala Thr Ala Val Pro Gly Tyr Ser Leu Thr | |
| 510 515 | |
| cagaatcttc aggtttgaga gaggtggggc caccagattc ttcatgtttc tgaaactttt | 2009 |
| tatTTTGGCA gaaggattgc cttccaagga aattattattt attgttttgt taacatatta | 2069 |
| atatttataa gggaaaacag cacataataa gggaaagctgg actagcccg agccttctca | 2129 |
| tttgggattt gtgctcataa ctgaaactcgt atcttttgtt caatggcat agctctgtaa | 2189 |

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tgtatgattg ggcttttgt tcagattgt aattcattaa tagatgaat atttatgcta 4649
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 35 40 45

Trp Met Ile Val Ala Gly Cys Phe Leu Val Thr Ile Cys Thr Arg Ala
 50 55 60

Val Thr Arg Cys Ile Ser Ile Phe Phe Val Glu Phe Gln Thr Tyr Phe
 65 70 75 80

Thr Gln Asp Tyr Ala Gln Thr Ala Trp Ile His Ser Ile Val Asp Cys
 85 90 95

Val Thr Met Leu Cys Ala Pro Leu Gly Ser Val Val Ser Asn His Leu
 100 105 110

Ser Cys Gln Val Gly Ile Met Leu Gly Gly Leu Leu Ala Ser Thr Gly
 115 120 125

Leu Ile Leu Ser Ser Phe Ala Thr Ser Leu Lys His Leu Tyr Leu Thr
 130 135 140

Leu Gly Val Leu Thr Gly Leu Gly Phe Ala Leu Cys Tyr Ser Pro Ala
 145 150 155 160

Ile Ala Met Val Gly Lys Tyr Phe Ser Arg Arg Lys Ala Leu Ala Tyr
 165 170 175

Gly Ile Ala Met Ser Gly Ser Gly Ile Gly Thr Phe Ile Leu Ala Pro
 180 185 190

Val Val Gln Leu Leu Ile Glu Gln Phe Ser Trp Arg Gly Ala Leu Leu
 195 200 205

Ile Leu Gly Gly Phe Val Leu Asn Leu Cys Val Cys Gly Ala Leu Met
 210 215 220

Arg Pro Ile Thr Leu Lys Glu Asp His Thr Thr Pro Glu Gln Asn His
 225 230 235 240

Val Cys Arg Thr Gln Lys Glu Asp Ile Lys Arg Val Ser Pro Tyr Ser
 245 250 255

160 200 PCT FINAL.ST25

Ser Leu Thr Lys Glu Trp Ala Gln Thr Cys Leu Cys Cys Cys Leu Gln
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Gln Glu Tyr Ser Phe Leu Leu Met Ser Asp Phe Val Val Leu Ala Val
275 280 285

Ser Val Leu Phe Met Ala Tyr Gly Cys Ser Pro Leu Phe Val Tyr Leu
290 295 300

Val Pro Tyr Ala Leu Ser Val Gly Val Ser His Gln Gln Ala Ala Phe
305 310 315 320

Leu Met Ser Ile Leu Gly Val Ile Asp Ile Ile Gly Asn Ile Thr Phe
325 330 335

Gly Trp Leu Thr Asp Arg Arg Cys Leu Lys Asn Tyr Gln Tyr Val Cys
340 345 350

Tyr Leu Phe Ala Val Gly Met Asp Gly Leu Cys Tyr Leu Cys Leu Pro
355 360 365

Met Leu Gln Ser Leu Pro Leu Leu Val Pro Phe Ser Cys Thr Phe Gly
370 375 380

Tyr Phe Asp Gly Ala Tyr Val Thr Leu Ile Pro Val Val Thr Thr Glu
385 390 395 400

Ile Val Gly Thr Thr Ser Leu Ser Ser Ala Leu Gly Val Val Tyr Phe
405 410 415

Leu His Ala Val Pro Tyr Leu Val Ser Pro Pro Ile Ala Gly Arg Leu
420 425 430

Val Asp Thr Thr Gly Ser Tyr Thr Ala Ala Phe Leu Leu Cys Gly Phe
435 440 445

Ser Met Ile Phe Ser Ser Val Leu Leu Gly Phe Ala Arg Leu Ile Lys
450 455 460

Arg Met Arg Lys Thr Gln Leu Gln Phe Ile Ala Lys Glu Ser Asp Pro
465 470 475 480

Lys Leu Gln Leu Trp Thr Asn Gly Ser Val Ala Tyr Ser Val Ala Arg
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Glu Leu Asp Gln Lys His Gly Glu Pro Val Ala Thr Ala Val Pro Gly
500 505 510

Tyr Ser Leu Thr
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| tgc cct gcc ctc agc agg ctg gtt ccc aga ggc ttt ggg act gag atg Cys Pro Ala Leu Ser Arg Leu Val Pro Arg Gly Phe Gly Thr Glu Met 20 25 30 | 155 |
| tgg act ctc ttt gcc ctt tct gga ccc ctg ttc ctg ttc cag gtg ctg Trp Thr Leu Phe Ala Leu Ser Gly Pro Leu Phe Leu Phe Gln Val Leu 35 40 45 | 203 |
| act ttt atg atc tac atc gtg agc act gtg ttc tgc ggg cac ctg ggc Thr Phe Met Ile Tyr Ile Val Ser Thr Val Phe Cys Gly His Leu Gly 50 55 60 | 251 |
| aag gtg gag ctg gca tcg gtg acc ctc gcg gtg gcc ttt gtc aat gtc Lys Val Glu Leu Ala Ser Val Thr Leu Ala Val Ala Phe Val Asn Val 65 70 75 | 299 |
| tgc gga gtt tct gta gga gtt ggt ttg tct tcg gca tgt gac acc ttg Cys Gly Val Ser Val Gly Val Leu Ser Ser Ala Cys Asp Thr Leu 80 85 90 95 | 347 |
| atg tct cag agc ttc ggc agc ccc aac aag aag cac gtg ggc gtg atc Met Ser Gln Ser Phe Gly Ser Pro Asn Lys Lys His Val Gly Val Ile 100 105 110 | 395 |
| ctg cag cgg ggc gcg ctg gtc ctg ctc tgc tgc ctc cct tgc tgg Leu Gln Arg Gly Ala Leu Val Leu Leu Cys Cys Leu Pro Cys Trp 115 120 125 | 443 |
| gcg ctc ttc ctc aac acc cag cac atc ctg ctg ctc ttc cgg cag gac Ala Leu Phe Leu Asn Thr Gln His Ile Leu Leu Leu Phe Arg Gln Asp 130 135 140 | 491 |
| ccg gac gtg tcc agg ttg acc cag gac tat gta atg att ttc att cca Pro Asp Val Ser Arg Leu Thr Gln Asp Tyr Val Met Ile Phe Ile Pro 145 150 155 | 539 |
| gga ctt ccg gtg att ttt ctt tac aat ctg ctg gca aaa tat ttg caa Gly Leu Pro Val Ile Phe Leu Tyr Asn Leu Leu Ala Lys Tyr Leu Gln 160 165 170 175 | 587 |
| aat cag aag atc acc tgg ccc caa gtc ctc agt ggt gtg gtc ggc aac Asn Gln Lys Ile Thr Trp Pro Gln Val Leu Ser Gly Val Val Gly Asn 180 185 190 | 635 |
| tgt gtc aac ggt gtg gcc aac tat gcc ctg gtt tct gtg ctg aac ctg Cys Val Asn Gly Val Ala Asn Tyr Ala Leu Val Ser Val Leu Asn Leu 195 200 205 | 683 |
| ggg gtc agg ggc tcc gcc tat gcc aac atc atc tcc cag ttt gca cag Gly Val Arg Gly Ser Ala Tyr Ala Asn Ile Ser Gln Phe Ala Gln 210 215 220 | 731 |
| acc gtc ttc ctc ctt ctc tac att gtg ctg aag aag ctg cac ctg gag Thr Val Phe Leu Leu Tyr Ile Val Leu Lys Lys Leu His Leu Glu 225 230 235 | 779 |
| acg tgg gca ggt tgg tcc agc cag tgc ctg cag gac tgg ggc ccc ttc Thr Trp Ala Gly Trp Ser Ser Gln Cys Leu Gln Asp Trp Gly Pro Phe 240 245 250 255 | 827 |
| ttc tcc ctg gct gtc ccc agc atg ctc atg atc tgc ttt gat ggg tgg Phe Ser Leu Ala Val Pro Ser Met Leu Met Ile Cys Val Glu Trp Trp 260 265 270 | 875 |
| gcc tat gag atc ggg agc ttc ctc atg ggg ctg ctc agt gtg gtc gat Ala Tyr Glu Ile Gly Ser Phe Leu Met Gly Leu Leu Ser Val Val Asp 275 280 285 | 923 |
| ctc tct gcc cag gtc atc tac gag gtg gcc act gtg acc tac atg Leu Ser Ala Gln Ala Val Ile Tyr Glu Val Ala Thr Val Thr Tyr Met 290 295 300 | 971 |
| att ccc ttg ggg ctc agc atc ggg gtc tgc ttt gca gtg ggg atg gct | 1019 |

160 200 PCT FINAL.ST25

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| Ile Pro Leu Gly Leu Ser Ile Gly Val Cys Val Arg Val Gly Met Ala | | | |
| 305 | 310 | 315 | |
| ctg ggg gct gcg gat act gtg cag gcc aag cgc tcg gcc gtc tcg ggc | | | 1067 |
| Leu Gly Ala Ala Asp Thr Val Gln Ala Lys Arg Ser Ala Val Ser Gly | | | |
| 320 | 325 | 330 | 335 |
| gtg ctc agc ata gtt ggc att tcc ctg gtc ctg ggc acc ctg ata agc | | | 1115 |
| Val Leu Ser Ile Val Gly Ile Ser Leu Val Leu Gly Thr Leu Ile Ser | | | |
| 340 | 345 | 350 | |
| atc ctg aaa aat cag ctg ggg cat att ttt acc aat gat gaa gat gtc | | | 1163 |
| Ile Leu Lys Asn Gln Leu Gly His Ile Phe Thr Asn Asp Glu Asp Val | | | |
| 355 | 360 | 365 | |
| att gcc ctg gtg agc cag gtc ttg ccg gtt tat agt gtc ttt cac gtg | | | 1211 |
| Ile Ala Leu Val Ser Gln Val Leu Pro Val Tyr Ser Val Phe His Val | | | |
| 370 | 375 | 380 | |
| ttt gag gcc atc tgt tgt gtc tat ggc gga gtt ctg aga gga act ggg | | | 1259 |
| Phe Glu Ala Ile Cys Cys Val Tyr Gly Gly Val Leu Arg Gly Thr Gly | | | |
| 385 | 390 | 395 | |
| aag cag gcc ttt ggt gcc gct gtg aat gcc atc aca tat tac atc atc | | | 1307 |
| Lys Gln Ala Phe Gly Ala Ala Val Asn Ala Ile Thr Tyr Tyr Ile Ile | | | |
| 400 | 405 | 410 | 415 |
| ggc cta cca ctg ggc atc ctt ctg acc ttt gtg gtc aga atg aga atc | | | 1355 |
| Gly Leu Pro Leu Gly Ile Leu Leu Thr Phe Val Val Arg Met Arg Ile | | | |
| 420 | 425 | 430 | |
| atg ggc ctc tgg ctg ggc atg ctg gcc tgt gtc ttc ctg gca act gct | | | 1403 |
| Met Gly Leu Trp Leu Gly Met Leu Ala Cys Val Phe Leu Ala Thr Ala | | | |
| 435 | 440 | 445 | |
| gcc ttt gtt gct tat act gcc cgg ctg gac tgg aag ctt gct gca gag | | | 1451 |
| Ala Phe Val Ala Tyr Thr Ala Arg Leu Asp Trp Lys Leu Ala Ala Glu | | | |
| 450 | 455 | 460 | |
| gag gct aag aaa cat tca ggc cgg cag cag cag cag aga gca gag agc | | | 1499 |
| Glu Ala Lys Lys His Ser Gly Arg Gln Gln Gln Arg Ala Glu Ser | | | |
| 465 | 470 | 475 | |
| act gca acc aga cct ggg cct gag aaa gca gtc cta tct tca gtg gct | | | 1547 |
| Thr Ala Thr Arg Pro Gly Pro Glu Lys Ala Val Leu Ser Ser Val Ala | | | |
| 480 | 485 | 490 | 495 |
| aca ggc agt tcc cct ggc att acc ttg aca acg tat tca agg tct gag | | | 1595 |
| Thr Gly Ser Ser Pro Gly Ile Thr Leu Thr Tyr Ser Arg Ser Glu | | | |
| 500 | 505 | 510 | |
| tgc cac gtg gac ttc ttc agg act cca gag gag gcc cac gcc ctt tca | | | 1643 |
| Cys His Val Asp Phe Arg Thr Pro Glu Glu Ala His Ala Leu Ser | | | |
| 515 | 520 | 525 | |
| gct cct acc agc aga cta tca gtg aaa cag ctg gtc atc cgc cgt ggg | | | 1691 |
| Ala Pro Thr Ser Arg Leu Ser Val Lys Gln Leu Val Ile Arg Arg Gly | | | |
| 530 | 535 | 540 | |
| - gct gct ctg ggg gcg tca gcc aca ctg atg gtg ggg ctc acg gtc | | | 1739 |
| Ala Ala Leu Gly Ala Ala Ser Ala Thr Leu Met Val Gly Leu Thr Val | | | |
| 545 | 550 | 555 | |
| agg atc cta gcc acc agg cac tagcaaagaa gcttggaaat agaaaagccag | | | 1790 |
| Arg Ile Leu Ala Thr Arg His | | | |
| 560 | 565 | | |
| gagtggtgtt cccagtatg caaacacacc acggctgtgcc ctgaaaaaac accaatgggg | | | 1850 |
| tcttagtgcatg tgacactc ctcaaaaaaaaaa gaactttggc tgattccttg | | | 1910 |
| tggtgacact cagagggttc tgaacagact tgacaattct gttctggta agctggagtt | | | 1970 |
| ttcttctgtg acttggactg ctctacagaa gacatcagcc aactgcacga gtcagagtcc | | | 2030 |
| agggattgtc actattatta ataatgtaaa tggcttcaaa tgggacactg cagataaaat | | | 2090 |
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35 40 45

Phe Met Ile Tyr Ile Val Ser Thr Val Phe Cys Gly His Leu Gly Lys
50 55 60

Val Glu Leu Ala Ser Val Thr Leu Ala Val Ala Phe Val Asn Val Cys
65 70 75 80

Gly Val Ser Val Gly Val Gly Leu Ser Ser Ala Cys Asp Thr Leu Met
85 90 95

Ser Gln Ser Phe Gly Ser Pro Asn Lys Lys His Val Gly Val Ile Leu
100 105 110

Gln Arg Gly Ala Leu Val Leu Leu Cys Cys Leu Pro Cys Trp Ala
115 120 125

Leu Phe Leu Asn Thr Gln His Ile Leu Leu Phe Arg Gln Asp Pro
130 135 140

Asp Val Ser Arg Leu Thr Gln Asp Tyr Val Met Ile Phe Ile Pro Gly
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Leu Pro Val Ile Phe Leu Tyr Asn Leu Leu Ala Lys Tyr Leu Gln Asn
165 170 175

Gln Lys Ile Thr Trp Pro Gln Val Leu Ser Gly Val Val Gly Asn Cys
180 185 190

Val Asn Gly Val Ala Asn Tyr Ala Leu Val Ser Val Leu Asn Leu Gly
195 200 205

Val Arg Gly Ser Ala Tyr Ala Asn Ile Ile Ser Gln Phe Ala Gln Thr
210 215 220

Val Phe Leu Leu Tyr Ile Val Leu Lys Lys Leu His Leu Glu Thr
225 230 235 240

Trp Ala Gly Trp Ser Ser Gln Cys Leu Gln Asp Trp Gly Pro Phe Phe
245 250 255

Ser Leu Ala Val Pro Ser Met Leu Met Ile Cys Val Glu Trp Trp Ala
260 265 270

Tyr Glu Ile Gly Ser Phe Leu Met Gly Leu Leu Ser Val Val Asp Leu
275 280 285

16U 200 PCT FINAL.ST25

Ser Ala Gln Ala Val Ile Tyr Glu Val Ala Thr Thr Tyr Met Ile
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Pro Leu Gly Leu Ser Ile Gly Val Cys Val Arg Val Gly Met Ala Leu
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Gly Ala Ala Asp Thr Val Gln Ala Lys Arg Ser Ala Val Ser Gly Val
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Leu Ser Ile Val Gly Ile Ser Leu Val Leu Gly Thr Leu Ile Ser Ile
 340 345 350

Leu Lys Asn Gln Leu Gly His Ile Phe Thr Asn Asp Glu Asp Val Ile
 355 360 365

Ala Leu Val Ser Gln Val Leu Pro Val Tyr Ser Val Phe His Val Phe
 370 375 380

Glu Ala Ile Cys Cys Val Tyr Gly Gly Val Leu Arg Gly Thr Gly Lys
 385 390 395 400

Gln Ala Phe Gly Ala Ala Val Asn Ala Ile Thr Tyr Tyr Ile Ile Gly
 405 410 415

Leu Pro Leu Gly Ile Leu Leu Thr Phe Val Val Arg Met Arg Ile Met
 420 425 430

Gly Leu Trp Leu Gly Met Leu Ala Cys Val Phe Leu Ala Thr Ala Ala
 435 440 445

Phe Val Ala Tyr Thr Ala Arg Leu Asp Trp Lys Leu Ala Ala Glu Glu
 450 455 460

Ala Lys Lys His Ser Gly Arg Gln Gln Gln Arg Ala Glu Ser Thr
 465 470 475 480

Ala Thr Arg Pro Gly Pro Glu Lys Ala Val Leu Ser Ser Val Ala Thr
 485 490 495

Gly Ser Ser Pro Gly Ile Thr Leu Thr Thr Tyr Ser Arg Ser Glu Cys
 500 505 510

His Val Asp Phe Phe Arg Thr Pro Glu Glu Ala His Ala Leu Ser Ala
 515 520 525

Pro Thr Ser Arg Leu Ser Val Lys Gln Leu Val Ile Arg Arg Gly Ala
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Gly Gln Glu Gly Phe Glu Ala Ser Ser Ala Pro Arg Asn Ile Pro Ser
10 15 20

ggg gag ctg gac agc aac cct gac cct ggc acc ggc ccc agc cct gat 149
Gly Glu Leu Asp Ser Asn Pro Asp Pro Gly Thr Gly Pro Ser Pro Asp
25 30 35

ggc ccc tca gac aca gag agc aag gaa ctg gga gta ccc aaa gac cct 197
Gly Pro Ser Asp Thr Glu Ser Lys Glu Leu Gly Val Pro Lys Asp Pro
40 45 50

ctg ctc ttc att cag ctg aat gag ctg ctg ggc tgg ccc cag gcg ctg 245
Leu Leu Phe Ile Gln Leu Asn Glu Leu Leu Gly Trp Pro Gln Ala Leu
55 60 65 70

gag tgg aga gag aca ggc agc tcc tct gca tct ctg ctc ctg gac atg 293
Glu Trp Arg Glu Thr Gly Ser Ser Ala Ser Leu Leu Leu Asp Met
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gga gaa atg ccc tca ata aca ctg tct acc cac ctt cat cac agg tgg 341
Gly Glu Met Pro Ser Ile Thr Leu Ser Thr His Leu His His Arg Trp
90 95 100

gta ctg ttt gag gag aag ttg gag gtg gct gca ggc cgg tgg agt gcc 389
Val Leu Phe Glu Glu Lys Leu Glu Val Ala Ala Gly Arg Trp Ser Ala
105 110 115

ccc cac gtg ccc acc ctg gca ctg ccc agc ctc cag aag ctc cgc agc 437
Pro His Val Pro Thr Leu Ala Leu Pro Ser Leu Gln Lys Leu Arg Ser
120 125 130

ctg ctg gcc gag ggc ctt gta ctg ctg gac tgc cca gct cag agc ctc 485
Leu Leu Ala Glu Gly Leu Val Leu Leu Asp Cys Pro Ala Gln Ser Leu
135 140 145 150

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Leu Glu Leu Val Glu Gln Val Thr Arg Val Glu Ser Leu Ser Pro Glu
155 160 165

ctg aga ggg cag ttg cag gcc ttg ctg ctg cag aga ccc cag cat tac 581
Leu Arg Gly Gln Leu Gln Ala Leu Leu Gln Arg Pro Gln His Tyr
170 175 180

aac cag acc aca ggc acc agg ccc tgc tgg ggc tct act cat cca aga 629
Asn Gln Thr Thr Gly Thr Arg Pro Cys Trp Gly Ser Thr His Pro Arg
185 190 195

aag gct tct gac aat gag gaa gcc ccc ctg agg gaa cag tgt cag aac 677
Lys Ala Ser Asp Asn Glu Glu Ala Pro Leu Arg Glu Gln Cys Gln Asn
200 205 210

ccc ctg aga cag aag cta cct cca gga gct gag gca ggg act gtg ctg 725
Pro-Leu Arg Gln-Lys Leu Pro Pro Gly Ala Glu Ala Gly Thr Val Leu
215 220 225 230

gca ggg gag ctg ggc ttc ctg gca cag cca ctg gga gcc ttt gtt cga 773
Ala Gly Glu Leu Gly Phe Leu Ala Gln Pro Leu Gly Ala Phe Val Arg
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Leu Arg Asn Pro Val Val Leu Gly Ser Leu Thr Glu Val Ser Leu Pro
250 255 260

agc agg ttt ttc tgc ctt ctc ctg ggc ccc tgt atg ctg gga aag ggc 869
Ser Arg Phe Phe Cys Leu Leu Gly Pro Cys Met Leu Gly Lys Gly
265 270 275

tac cat gag atg gga cgg gca gca gct gtc ctc ctc agt gac ccg caa 917
Tyr His Glu Met Gly Arg Ala Ala Val Leu Ser Asp Pro Gln

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| ttc cag tgg tca gtt cgt cgg gcc agc aac ctt cat gac ctt ctg gca Phe Gln Trp Ser Val Arg Arg Ala Ser Asn Leu His Asp Leu Leu Ala 295 300 305 310 | | | 965 |
| gcc ctg gat gca ttc cta gag gag gtg aca gtg ctt ccc cca ggt cgg Ala Leu Asp Ala Phe Leu Glu Glu Val Thr Val Leu Pro Pro Gly Arg 315 320 325 | | | 1013 |
| tgg gac cca aca gcc cgg att ccc ccg ccc aaa tgt ctg cca tct cag Trp Asp Pro Thr Ala Arg Ile Pro Pro Lys Cys Leu Pro Ser Gln 330 335 340 | | | 1061 |
| cac aaa agg ctt ccc tcg caa cag cgg gag atc aga ggt ccc gcc gtc His Lys Arg Leu Pro Ser Gln Gln Arg Glu Ile Arg Gly Pro Ala Val 345 350 355 | | | 1109 |
| ccg cgc ctg acc tcg gct gag gac agg cac cgc cat ggg cca cac gca Pro Arg Leu Thr Ser Ala Glu Asp Arg His Arg His Gly Pro His Ala 360 365 370 | | | 1157 |
| cac agc ccg gag ttg cag cgg acc ggc agg ctg ttt ggg ggc ctt atc His Ser Pro Glu Leu Gln Arg Thr Gly Arg Leu Phe Gly Gly Leu Ile 375 380 385 390 | | | 1205 |
| cag gac gtg cgc agg aag gtc ccg tgg tac ccc agc gat ttc ttg gac Gln Asp Val Arg Arg Lys Val Pro Trp Tyr Pro Ser Asp Phe Leu Asp 395 400 405 | | | 1253 |
| gcc ctg cat ctc cag tgc ttc tcg gcc gta ctc tac att tac ctg gcc Ala Leu His Leu Gln Cys Phe Ser Ala Val Leu Tyr Ile Tyr Leu Ala 410 415 420 | | | 1301 |
| act gtc act aat gcc atc act ttt ggg ggt ctg ctg gga gat gcc act Thr Val Thr Asn Ala Ile Thr Phe Gly Gly Leu Leu Gly Asp Ala Thr 425 430 435 | | | 1349 |
| gat ggt gcc cag gga gtg ctg gaa agt ttc ctg ggc aca gca gtg gct Asp Gly Ala Gln Gly Val Leu Glu Ser Phe Leu Gly Thr Ala Val Ala 440 445 450 | | | 1397 |
| gga gct gcc ttc tgc ctg atg gca ggc cag ccc ctc acc att ctg agc Gly Ala Ala Phe Cys Leu Met Ala Gly Gln Pro Leu Thr Ile Leu Ser 455 460 465 470 | | | 1445 |
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| ctg gtg cgc tac ttc acc cgc ttc act gag gaa ggt ttc tgt gcc ctc Leu Val Arg Tyr Phe Thr Arg Phe Thr Glu Glu Gly Phe Cys Ala Leu 520 525 530 | | | 1637 |
| atc agc ctc atc ttc atc tac gat gct gtg ggc aaa atg ctg aac ttg Ile Ser Leu Ile Phe Ile Tyr Asp Ala Val Gly Lys Met Leu Asn Leu 535 540 545 550 | | | 1685 |
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| ctc tgc caa tac cca ggc cca gga gga aat gag tct caa tgg ata agg Leu Cys Gln Tyr Pro Gly Pro Gly Gly Asn Glu Ser Gln Trp Ile Arg 570 575 580 | | | 1781 |
| aca agg cca aaa gac aga gac gac att gta agc atg gac tta ggc ctg Thr Arg Pro Lys Asp Arg Asp Ile Val Ser Met Asp Leu Gly Leu 585 590 595 | | | 1829 |
| atc aat gca tcc ttg ctg ccg cca cct gag tgc acc cgg cag gga ggc | | | 1877 |

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| | | | |
|---|-----|------|-----|
| Ile Asn Ala Ser Leu Leu Pro Pro Pro Glu Cys Thr Arg Gln Gly Gly | | | |
| 600 | 605 | 610 | |
| | | | |
| Cac cct cgt ggc cct ggc tgt cat aca gtc cca gac att gcc ttc ttc | | 1925 | |
| His Pro Arg Gly Pro Gly Cys His Thr Val Pro Asp Ile Ala Phe Phe | | | |
| 615 | 620 | 625 | 630 |
| | | | |
| tcc ctt Ctc ctc ttc ctt act tct ttc ttc ttt gct atg gcc ctc aag | | 1973 | |
| Ser Leu Leu Phe Leu Thr Ser Phe Phe Phe Ala Met Ala Leu Lys | | | |
| 635 | 640 | 645 | |
| | | | |
| tgt gta aag acc agc cgc ttc ttc ccc tct gtg gtg cgc aaa ggg ctc | | 2021 | |
| Cys Val Lys Thr Ser Arg Phe Phe Pro Ser Val Val Arg Lys Gly Leu | | | |
| 650 | 655 | 660 | |
| | | | |
| agc gac ttc tcc tca gtc ctg gcc atc ctg ctc ggc tgt ggc ctt gat | | 2069 | |
| Ser Asp Phe Ser Ser Val Leu Ala Ile Leu Leu Gly Cys Gly Leu Asp | | | |
| 665 | 670 | 675 | |
| | | | |
| gct ttc ctg ggc cta aca cca aag ctc atg gta ccc aga gag ttc | | 2117 | |
| Ala Phe Leu Gly Leu Ala Thr Pro Lys Leu Met Val Pro Arg Glu Phe | | | |
| 680 | 685 | 690 | |
| | | | |
| aag ccc aca ctc cct ggg cgt ggc tgg ctg gtg tca cct ttt gga gcc | | 2165 | |
| Lys Pro Thr Leu Pro Gly Arg Gly Trp Leu Val Ser Pro Phe Gly Ala | | | |
| 695 | 700 | 705 | 710 |
| | | | |
| aac ccc tgg tgg tgg agt gtg gca gct gcc ctg cct gcc ctg ctg ctg | | 2213 | |
| Asn Pro Trp Trp Trp Ser Val Ala Ala Leu Pro Ala Leu Leu Leu | | | |
| 715 | 720 | 725 | |
| | | | |
| tct atc ctc atc ttc atg gac caa cag atc aca gca gtc atc ctc aac | | 2261 | |
| Ser Ile Leu Ile Phe Met Asp Gln Gln Ile Thr Ala Val Ile Leu Asn | | | |
| 730 | 735 | 740 | |
| | | | |
| cgc atg gaa tac aga ctg cag aag gga gct ggc ttc cac ctg gac ctc | | 2309 | |
| Arg Met Glu Tyr Arg Leu Gln Lys Gly Ala Gly Phe His Leu Asp Leu | | | |
| 745 | 750 | 755 | |
| | | | |
| ttc tgt gtc gct gtg ctg atg cta ctc aca tca gcg ctt gga ctg cct | | 2357 | |
| Phe Cys Val Ala Val Leu Met Leu Leu Thr Ser Ala Leu Gly Leu Pro | | | |
| 760 | 765 | 770 | |
| | | | |
| tgg tat gtc tca gcc act gtc atc tcc ctg gct cac atg gac agt ctt | | 2405 | |
| Trp Tyr Val Ser Ala Thr Val Ile Ser Leu Ala His Met Asp Ser Leu | | | |
| 775 | 780 | 785 | 790 |
| | | | |
| Cgg aga gag agc aga gcc tgt gtc ccc ggg gag cgc ccc aac ttc ctg | | 2453 | |
| Arg Arg Glu Ser Arg Ala Cys Ala Pro Gly Glu Arg Pro Asn Phe Leu | | | |
| 795 | 800 | 805 | |
| | | | |
| ggg atc agg gaa cag agg ctg aca ggc ctg gtg gtc atc ctt aca | | 2501 | |
| Gly Ile Arg Glu Gln Arg Leu Thr Gly Leu Val Val Phe Ile Leu Thr | | | |
| 810 | 815 | 820 | |
| | | | |
| gga gcc tcc atc ttc ctg gca cct gtg ctc aag ttc att cca atg cct | | 2549 | |
| Gly Ala Ser Ile Phe Leu Ala Pro Val Leu Lys Phe Ile Pro Met Pro | | | |
| 825 | 830 | 835 | |
| | | | |
| gtg ctc tat ggc atc ttc ctg tat atg ggg gtg gca gcg ctc agc agc | | 2597 | |
| Val Leu Tyr Gly Ile Phe Leu Tyr Met Gly Val Ala Ala Leu Ser Ser | | | |
| 840 | 845 | 850 | |
| | | | |
| att cag ttc act aat agg gtg aag ctg ttg atg cca gca aaa cac | | 2645 | |
| Ile Gln Phe Thr Asn Arg Val Lys Leu Leu Met Pro Ala Lys His | | | |
| 855 | 860 | 865 | 870 |
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| cag cca gac ctg cta ctc ttg cgg cat gtg cct ctg acc agg gtc cac | | 2693 | |
| Gln Pro Asp Leu Leu Leu Arg His Val Pro Leu Thr Arg Val His | | | |
| 875 | 880 | 885 | |
| | | | |
| ctc ttc aca gcc atc cag ctt gcc tgt ctg ggg ctg ctt tgg ata atc | | 2741 | |
| Leu Phe Thr Ala Ile Gln Leu Ala Cys Leu Gly Leu Leu Trp Ile Ile | | | |
| 890 | 895 | 900 | |
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| aag tct acc cct gca gcc atc atc ttc ccc ctc atg ttg ctg ggc ctt | | 2789 | |
| Lys Ser Thr Pro Ala Ala Ile Ile Phe Pro Leu Met Leu Leu Gly Leu | | | |
| 905 | 910 | 915 | |

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| | |
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| gtg ggg gtc cga aag gcc ctg gag agg gtc ttc tca cca cag gaa ctc Val Gly Val Arg Lys Ala Leu Glu Arg Val Phe Ser Pro Gln Glu Leu 920 925 930 | 2837 |
| ctc tgg ctg gat gag ctg atg cca gag gag gag aga agc atc cct gag Leu Trp Leu Asp Glu Leu Met Pro Glu Glu Arg Ser Ile Pro Glu 935 940 945 950 | 2885 |
| aag ggg ctg gag cca gaa cac tca ttc agt gga agt gac agt gaa gat Lys Gly Leu Glu Pro Glu His Ser Phe Ser Gly Ser Asp Ser Glu Asp 955 960 965 | 2933 |
| tca gag ctg atg tat cag cca aag gct cca gaa atc aac att tct gtg Ser Glu Leu Met Tyr Gln Pro Lys Ala Pro Glu Ile Asn Ile Ser Val 970 975 980 | 2981 |
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| Thr Gly Pro Ser Pro Asp Gly Pro Ser Asp Thr Glu Ser Lys Glu Leu 35 40 45 | |
| Gly Val Pro Lys Asp Pro Leu Leu Phe Ile Gln Leu Asn Glu Leu Leu 50 55 60 | |
| Gly Trp Pro Gln Ala Leu Glu Trp Arg Glu Thr Gly Ser Ser Ser Ala 65 70 75 80 | |
| Ser Leu Leu Leu Asp Met Gly Glu Met Pro Ser Ile Thr Leu Ser Thr 85 90 95 | |
| His Leu His His Arg Trp Val Leu Phe Glu Glu Lys Leu Glu Val Ala 100 105 110 | |
| Ala Gly Arg Trp Ser Ala Pro His Val Pro Thr Leu Ala Leu Pro Ser 115 120 125 | |
| Leu Gln Lys Leu Arg Ser Leu Leu Ala Glu Gly Leu Val Leu Leu Asp 130 135 140 | |
| Cys Pro Ala Gln Ser Leu Leu Glu Leu Val Glu Gln Val Thr Arg Val 145 150 155 160 | |
| Glu Ser Leu Ser Pro Glu Leu Arg Gly Gln Leu Gln Ala Leu Leu Leu 165 170 175 | |
| Gln Arg Pro Gln His Tyr Asn Gln Thr Thr Gly Thr Arg Pro Cys Trp 180 185 190 | |
| Gly Ser Thr His Pro Arg Lys Ala Ser Asp Asn Glu Glu Ala Pro Leu | |

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195 200 205

Arg Glu Gln Cys Gln Asn Pro Leu Arg Gln Lys Leu Pro Pro Gly Ala
210 215 220

Glu Ala Gly Thr Val Leu Ala Gly Glu Leu Gly Phe Leu Ala Gln Pro
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245 250 255

Thr Glu Val Ser Leu Pro Ser Arg Phe Phe Cys Leu Leu Gly Pro
260 265 270

Cys Met Leu Gly Lys Gly Tyr His Glu Met Gly Arg Ala Ala Ala Val
275 280 285

Leu Leu Ser Asp Pro Gln Phe Gln Trp Ser Val Arg Arg Ala Ser Asn
290 295 300

Leu His Asp Leu Leu Ala Ala Leu Asp Ala Phe Leu Glu Glu Val Thr
305 310 315 320

Val Leu Pro Pro Gly Arg Trp Asp Pro Thr Ala Arg Ile Pro Pro Pro
325 330 335

Lys Cys Leu Pro Ser Gln His Lys Arg Leu Pro Ser Gln Gln Arg Glu
340 345 350

Ile Arg Gly Pro Ala Val Pro Arg Leu Thr Ser Ala Glu Asp Arg His
355 360 365

Arg His Gly Pro His Ala His Ser Pro Glu Leu Gln Arg Thr Gly Arg
370 375 380

Leu Phe Gly Gly Leu Ile Gln Asp Val Arg Arg Lys Val Pro Trp Tyr
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Pro Ser Asp Phe Leu Asp Ala Leu His Leu Gln Cys Phe Ser Ala Val
405 410 415

Leu Tyr Ile Tyr Leu Ala Thr Val Thr Asn Ala Ile Thr Phe Gly Gly
420 425 430

Leu Leu Gly Asp Ala Thr Asp Gly Ala Gln Gly Val Leu Glu Ser Phe
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Leu Gly Thr Ala Val Ala Gly Ala Ala Phe Cys Leu Met Ala Gly Gln
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Pro Leu Thr Ile Leu Ser Ser Thr Gly Pro Val Leu Val Phe Glu Arg
465 470 475 480

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485 490 495

Arg Leu Trp Val Gly Ile Trp Val Ala Thr Phe Cys Leu Val Leu Val
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16U 200 PCT FINAL.ST25
Ala Thr Glu Ala Ser Val Leu Val Arg Tyr Phe Thr Arg Phe Thr Glu
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Gly Lys Met Leu Asn Leu Thr His Thr Tyr Pro Ile Gln Lys Pro Gly
545 550 555 560

Ser Ser Ala Tyr Gly Cys Leu Cys Gln Tyr Pro Gly Pro Gly Asn
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Glu Ser Gln Trp Ile Arg Thr Arg Pro Lys Asp Arg Asp Asp Ile Val
580 585 590

Ser Met Asp Leu Gly Leu Ile Asn Ala Ser Leu Leu Pro Pro Pro Glu
595 600 605

Cys Thr Arg Gln Gly Gly His Pro Arg Gly Pro Gly Cys His Thr Val
610 615 620

Pro Asp Ile Ala Phe Phe Ser Leu Leu Leu Phe Leu Thr Ser Phe Phe
625 630 635 640

Phe Ala Met Ala Leu Lys Cys Val Lys Thr Ser Arg Phe Phe Pro Ser
645 650 655

Val Val Arg Lys Gly Leu Ser Asp Phe Ser Ser Val Leu Ala Ile Leu
660 665 670

Leu Gly Cys Gly Leu Asp Ala Phe Leu Gly Leu Ala Thr Pro Lys Leu
675 680 685

Met Val Pro Arg Glu Phe Lys Pro Thr Leu Pro Gly Arg Gly Trp Leu
690 695 700

Val Ser Pro Phe Gly Ala Asn Pro Trp Trp Trp Ser Val Ala Ala Ala
705 710 715 720

Leu Pro Ala Leu Leu Ser Ile Leu Ile Phe Met Asp Gln Gln Ile
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Thr Ala Val Ile Leu Asn Arg Met Glu Tyr Arg Leu Gln Lys Gly Ala
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Gly Phe His Leu Asp Leu Phe Cys Val Ala Val Leu Met Leu Leu Thr
755 760 765

Ser Ala Leu Gly Leu Pro Trp Tyr Val Ser Ala Thr Val Ile Ser Leu
770 775 780

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785 790 795 800

Glu Arg Pro Asn Phe Leu Gly Ile Arg Glu Gln Arg Leu Thr Gly Leu
805 810 815

Val Val Phe Ile Leu Thr Gly Ala Ser Ile Phe Leu Ala Pro Val Leu
820 825 830

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Lys Phe Ile Pro Met Pro Val Leu Tyr Gly Ile Phe Leu Tyr Met Gly
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Val Ala Ala Leu Ser Ser Ile Gln Phe Thr Asn Arg Val Lys Leu Leu
 850 855 860

Leu Met Pro Ala Lys His Gln Pro Asp Leu Leu Leu Leu Arg His Val
 865 870 875 880

Pro Leu Thr Arg Val His Leu Phe Thr Ala Ile Gln Leu Ala Cys Leu
 885 890 895

Gly Leu Leu Trp Ile Ile Lys Ser Thr Pro Ala Ala Ile Ile Phe Pro
 900 905 910

Leu Met Leu Leu Gly Leu Val Gly Val Arg Lys Ala Leu Glu Arg Val
 915 920 925

Phe Ser Pro Gln Glu Leu Leu Trp Leu Asp Glu Leu Met Pro Glu Glu
 930 935 940

Glu Arg Ser Ile Pro Glu Lys Gly Leu Glu Pro Glu His Ser Phe Ser
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Glu Ile Asn Ile Ser Val Asn
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 Met Ser Arg Ser Arg Leu Phe Ser Val Thr Ser Ala Ile Ser Thr Ile
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ggg atc ttg tgt ttg ccg cta ttc cag ttg gtg ctc tcg gac cta cca 155
 Gly Ile Leu Cys Leu Pro Leu Phe Gln Leu Val Leu Ser Asp leu Pro
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tgc gaa gaa gat gaa atg tgt gta aat tat aat gac caa cac cct aat 203
 Cys Glu Asp Glu Met Cys Val Asn Tyr Asn Asp Gln His Pro Asn
 35 40 45

ggc tgg tat atc tgg atc ctc ctg ctg gtt ttg gtg gcá gct ctt 251
 Gly Trp Tyr Ile Trp Ile Leu Leu Leu Val Leu Val Ala Ala Leu
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ctc tgt gga gct gtg gtc ctc tgc ctc cag tgc ttg ctg agg aga ccc 299
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 65 70 75 80

cga att gat tct cac agg cgc acc atg gca gtt ttt gct gtt gga gac 347
 Arg Ile Asp Ser His Arg Arg Thr Met Ala Val Phe Ala Val Gly Asp
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ttg gac tct att tat ggg aca gaa gca gct gtg agt cca act gtt gga 395

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|--|-----|-----|----|
| Leu Asp Ser Ile Tyr Gly Thr Glu Ala Ala Val Ser Pro Thr Val Gly | | | |
| 100 | 105 | 110 | |
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| att cac ctt caa act caa acc cct gac cta tat cct gtt cct gct cca | 443 | | |
| Ile His Leu Gln Thr Gln Thr Pro Asp Leu Tyr Pro Val Pro Ala Pro | | | |
| 115 | 120 | 125 | |
| | | | |
| tgt ttt ggc cct tta ggc tcc cca cct cca tat gaa gaa att gta aaa | 491 | | |
| Cys Phe Gly Pro Leu Gly Ser Pro Pro Tyr Glu Glu Ile Val Lys | | | |
| 130 | 135 | 140 | |
| | | | |
| aca acc tgatTTAGG tgtggattat caatttaa ^{AG} tattaacgac atctgtatt | 547 | | |
| Thr Thr | | | |
| 145 | | | |
| | | | |
| ccaaaacatc aaatttagga atagttattt cagttgttg aatgtccag agatctattc | 607 | | |
| ataatgtctg aggaaggaca attcgacaaa agaatggatg ttggaaaaaaa ttttggcat | 667 | | |
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| Gly Ile Leu Cys Leu Pro Leu Phe Gln Leu Val Leu Ser Asp Leu Pro | | | |
| 20 | 25 | 30 | |
| | | | |
| Cys Glu Glu Asp Glu Met Cys Val Asn Tyr Asn Asp Gln His Pro Asn | | | |
| 35 | 40 | 45 | |
| | | | |
| Gly Trp Tyr Ile Trp Ile Leu Leu Leu Val Leu Val Ala Ala Leu | | | |
| 50 | 55 | 60 | |
| | | | |
| Leu Cys Gly Ala Val Val Leu Cys Leu Gln Cys Trp Leu Arg Arg Pro | | | |
| 65 | 70 | 75 | 80 |
| | | | |
| Arg Ile Asp Ser His Arg Arg Thr Met Ala Val Phe Ala Val Gly Asp | | | |
| 85 | 90 | 95 | |
| | | | |
| Leu Asp Ser Ile Tyr Gly Thr Glu Ala Ala Val Ser Pro Thr Val Gly | | | |
| 100 | 105 | 110 | |
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| Ile His Leu Gln Thr Gln Thr Pro Asp Leu Tyr Pro Val Pro Ala Pro | | | |
| 115 | 120 | 125 | |
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| Cys Phe Gly Pro Leu Gly Ser Pro Pro Pro Tyr Glu Glu Ile Val Lys | | | |
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| Ser Gly Arg Leu Glu Asp Phe Pro Val Asn Val Phe Ser Val Thr Pro | | |
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| | | |
| tac aca ccc acc gct gac atc cag gtg tcc gat gat gac aag gcg | 151 | |
| Tyr Thr Pro Ser Thr Ala Asp Ile Gln Val Ser Asp Asp Lys Ala | | |
| 25 30 35 | | |
| | | |
| ggg gcc acc ttg ctc ttc tca ggc atc ttt ctg gga ctg gtg ggg atc | 199 | |
| Gly Ala Thr Leu Leu Phe Ser Gly Ile Phe Leu Gly Leu Val Gly Ile | | |
| 40 45 50 | | |
| | | |
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| Glu Trp Thr Gln Leu Leu Gly Pro Val Leu Leu Ser Val Gly Val Thr | | |
| 70 75 80 | | |
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| Phe Ile Leu Ile Ala Val Cys Lys Phe Lys Met Leu Ser Cys Gln Leu | | |
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| Gly Pro Ser Phe Val Phe Thr Gly Ile Asn Gln Pro Ile Thr Phe His | | |
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| Gly Ala Thr Val Val Gln Tyr Ile Pro Pro Tyr Gly Ser Pro Glu | | |
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| Pro Met Gly Ile Asn Thr Ser Tyr Leu Gln Ser Val Val Ser Pro Cys | | |
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| Gly Leu Ile Thr Ser Gly Gly Ala Ala Ala Met Ser Ser Pro Pro | | |
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| caa tac tac acc atc tac cct caa gat aac tct gca ttt gtg gtt gat | 631 | |
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| Asp Val Asp Gln Leu Glu Glu Ile Tyr Ser Leu Pro Arg | | |
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| ggg aat ggc cag gca gaa gcc aag gag gaa gca gag ggc tca ggg cag Gly Asn Gly Gln Ala Glu Ala Lys Glu Glu Ala Glu Gly Ser Gly Gln 370 375 380 | 1152 | |
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| cgt cgg agg agc agc aag cgg gct gaa gca cca cag ggc tgc agc tgt Arg Arg Arg Ser Ser Lys Arg Ala Glu Ala Pro Gln Gly Cys Ser Cys 405 410 415 | 1248 | |
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| gac aca aag ggt gca gcc gaa aga gcc gcc tcc ccg cag aca ggg ccg Asp Thr Lys Gly Ala Ala Glu Arg Ala Ala Ser Pro Gln Thr Gly Pro 660 665 670 | 2016 |
| tgg ccc tcc acc cga ggc ttc agc cgg aag gag agc ctt ctg cag ata Trp Pro Ser Thr Arg Gly Phe Ser Arg Lys Glu Ser Leu Leu Gln Ile 675 680 685 | 2064 |
| gcg gag aac cca gag ctg cag ctg cag cca gat ggc ttc ccg ctc ccc Ala Glu Asn Pro Glu Leu Gln Leu Gln Pro Asp Gly Phe Arg Leu Pro 690 695 700 | 2112 |
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| Ser | Gly | Cys | Gln | Gly | Pro | Gly | His | Gln | Pro | Ser | Ser | Arg | Val | Phe | Cys | |
| 865 | | | | | 870 | | | | | 875 | | | | | 880 | |
| tac | aac | ccg | ctc | acg | ggg | atc | tgg | agc | gag | gtg | tgc | ccg | ctg | aac | cag | 2688 |
| Tyr | Asn | Pro | Leu | Thr | Gly | Ile | Trp | Ser | Glu | Val | Cys | Pro | Leu | Asn | Gln | |
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| gcc | cg | ccg | cac | tgc | cg | ctg | gtg | gcc | ctg | gt | g | gg | cac | ctg | tat | 2736 |
| Ala | Arg | Pro | His | Cys | Arg | Leu | Val | Ala | Leu | Asp | Gly | His | Leu | Tyr | Ala | |
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| atc | ggc | gga | gag | tgt | ctg | aac | tcg | gtg | gag | cgt | tac | gac | ccc | cgc | ctg | 2784 |
| Ile | Gly | Gly | Gly | Cys | Leu | Asn | Ser | Val | Glu | Arg | Tyr | Asp | Pro | Arg | Leu | |
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| gac | cg | tgg | gac | ttt | gcc | ccg | ccg | ctc | ccc | agt | gac | acg | ttc | gcc | ctg | 2832 |
| Asp | Arg | Trp | Asp | Phe | Ala | Pro | Pro | Leu | Pro | Ser | Asp | Thr | Phe | Ala | Leu | |
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| gcg | cac | acg | gcc | acg | gtg | cgt | gcc | aag | gaa | atc | ttc | gtc | acc | ggc | ggc | 2880 |
| Ala | His | Thr | Ala | Thr | Val | Arg | Ala | Lys | Glu | Ile | Phe | Val | Thr | Gly | Gly | |
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| Trp | Ala | Gly | Pro | Thr | Gly | Gly | Ser | Lys | Asp | Arg | Thr | Ala | Glu | Met | Val | |
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| gcg | gtc | aac | ggc | ttt | ctc | tac | cgc | ttt | gac | ctc | aac | cgc | agc | ctg | ggc | 3024 |
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| Cys | Ala | Thr | Tyr | Arg | Thr | Pro | Tyr | Pro | Asp | Ala | Phe | Gln | Cys | Ala | | |
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| Val | Val | Asp | Asn | Leu | Ile | Tyr | Cys | Val | Gly | Arg | Arg | Ser | Thr | Leu | | |
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| tgc | tcc | cta | gca | gac | tct | gtc | tca | ccc | aga | tct | gt | gcc | gtc | tcc | 3204 | |
| Cys | Phe | Leu | Ala | Asp | Ser | Val | Ser | Pro | Arg | Ser | Val | Ala | Val | Phe | | |
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| Leu | Ser | Gly | Ser | Trp | Gly | Asn | His | His | Gln | Ser | Ala | Leu | Gln | Gly | | |
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| Asp | Ser | Ile | Ile | Cys | Pro | Pro | Cys | Ala | Arg | Trp | Ser | Gln | Leu | Asp | | |
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| Pro | Val | Ser | Thr | Glu | Ala | Ala | Gly | Ala | Gln | Ala | Val | Gly | Leu | Val | | |
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| Asp | Ile | Arg | Gly | Glu | Leu | Ala | Leu | Asp | His | Arg | Arg | Pro | Pro | Ser | | |
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Cys Ser Thr Glu Val Asn Phe Gly Ser Arg Gln Gln Gly Lys Leu Asn
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Pro Ser Ala Gln Gln Asp Pro Gly Thr Gly Pro Tyr Trp Ala Ile Ile
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Asn Gln Ile Leu Asp Ile Pro Gln Pro Gln Val Gly Trp Arg Ser Met
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Phe Pro Arg Gly Ala Glu Ala Asp Trp His Leu Asp Met Gln Leu
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Ala Tyr Arg Leu Tyr Lys Ser Arg Pro Ala Pro Ala Gln Arg Trp Gly
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Glu Asn Pro Arg Gly Pro Tyr Val Leu Val Thr Gly Ala Thr Ser Thr
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Tyr Asn Pro Leu Thr Gly Ile Trp Ser Glu Val Cys Pro Leu Asn Gln
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Ala Arg Pro His Cys Arg Leu Val Ala Leu Asp Gly His Leu Tyr Ala
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Ala His Thr Ala Thr Val Arg Ala Lys Glu Ile Phe Val Thr Gly Gly
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| | |
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| ctg gaa cag acc cca gtg aag gag ctg gtg agc ttc aag tgg aac aag Leu Glu Gln Thr Pro Val Lys Glu Leu Val Ser Phe Lys Trp Asn Lys 310 315 320 | 1318 |
| tat ggc cgg ccg tac ttc tgc atc ctg gct gcc ttg tac ctg ctc tac Tyr Gly Arg Pro Tyr Phe Cys Ile Leu Ala Ala Leu Tyr Leu Leu Tyr 325 330 335 | 1366 |
| atg atc tgc ttt acc acg tgc tgc gtc tac cgc ccc ctt aag ttt cgt Met Ile Cys Phe Thr Thr Cys Cys Val Tyr Arg Pro Leu Lys Phe Arg 340 345 350 355 | 1414 |
| ggc ggc aac cgc act cat tct cga gac atc acc atc ctc cag caa aaa Gly Gly Asn Arg Thr His Ser Arg Asp Ile Thr Ile Leu Gln Gln Lys 360 365 370 | 1462 |
| cta cta cag gag gcc tat gag aca cgt gaa gat atc atc agg ctg gtg Leu Leu Gln Glu Ala Tyr Glu Thr Arg Glu Asp Ile Ile Arg Leu Val 375 380 385 | 1510 |
| ggg gag ctg gtg agc atc gtt ggg gct gtg atc atc ctg ctc cta gag Gly Glu Leu Val Ser Ile Val Gly Ala Val Ile Ile Leu Leu Glu 390 395 400 | 1558 |
| att cca gac atc ttc agg gtt ggt gcc tct cgc tat ttt gga aag acg Ile Pro Asp Ile Phe Arg Val Gly Ala Ser Arg Tyr Phe Gly Lys Thr 405 410 415 | 1606 |
| att ctt ggg ggg cca ttc cat gtc atc atc acc tat gcc tcc ctg Ile Leu Gly Gly Pro Phe His Val Ile Ile Ile Thr Tyr Ala Ser Leu 420 425 430 435 | 1654 |
| gtg ctg gtg acc atg gtg atg cgg ctc acc aac acc aat ggg gag gtg Val Leu Val Thr Met Val Met Arg Leu Thr Asn Thr Asn Gly Glu Val 440 445 450 | 1702 |
| gtg ccc atg tcc ttt gcc ctg gtg ggc tgg tgc agt gtc atg tat Val Pro Met Ser Phe Ala Leu Val Leu Gly Trp Cys Ser Val Met Tyr 455 460 465 | 1750 |
| tcc act cga gga ttc cag atg ctg ggt ccc ttc acc atc atg atc cag Phe Thr Arg Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln 470 475 480 | 1798 |
| aag atg att ttt gga gac cta atg cgt ttc tgc tgg ctg atg gct gtg Lys Met Ile Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val 485 490 495 | 1846 |
| gtc atc ttg gga ttt gcc tcc gcg ttc tat atc att ttc cag aca gag Val Ile Leu Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu 500 505 510 515 | 1894 |
| gac cca acc agt ctg ggg caa ttc tat gac tac ccc atg gca ctg ttc Asp Pro Thr Ser Leu Gly Gln Phe Tyr Asp Tyr Pro Met Ala Leu Phe 520 525 530 | 1942 |
| acc acc ttt gag ctt ttt ctc act gtt att gat gca cct gcc aac tac Thr Thr Phe Glu Leu Phe Leu Thr Val Ile Asp Ala Pro Ala Asn Tyr 535 540 545 | 1990 |
| gac gtg gac ttg ccc ttc atg ttc agc att gtc aac ttc gcc ttc gcc Asp Val Asp Leu Pro Phe Met Phe Ser Ile Val Asn Phe Ala Phe Ala 550 555 560 | 2038 |
| atc att gcc aca ctg ctc atg ctc aac ttg ttc atc gcc atg atg ggc Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Phe Ile Ala Met Met Gly | 2086 |

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565 570 575

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| gac acc cac tgg agg gtc gcc cag gag agg gat gag ctc tgg agg gcc Asp Thr His Trp Arg Val Ala Gln Glu Arg Asp Glu Leu Trp Arg Ala 580 585 590 595 | 2134 |
| cag gtc gtc acc aca gtc atg ctg gag cgg aag ctg cct cgc tgc Gln Val Val Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys 600 605 610 | 2182 |
| ctg tgg cct cgc tcc ggg atc tgt ggg tgc gaa ttc ggg ctg ggg gac Leu Trp Pro Arg Ser Gly Ile Cys Gly Cys Glu Phe Gly Leu Gly Asp 615 620 625 | 2230 |
| cgc tgg ttc ctg cgg gtt gag aac cac aat gat cag aat cct ctg cga Arg Trp Phe Leu Arg Val Glu Asn His Asn Asp Gln Asn Pro Leu Arg 630 635 640 | 2278 |
| gtg ctt cgc tat gtc gaa gtc ttc aag aac tca gac aag gag gat gac Val Leu Arg Tyr Val Glu Val Phe Lys Asn Ser Asp Lys Glu Asp Asp 645 650 655 | 2326 |
| cag gag cat cca tct gag aaa cag ccc tct ggg gct gag agt ggg act Gln Glu His Pro Ser Glu Lys Gln Pro Ser Gly Ala Glu Ser Gly Thr 660 665 670 675 | 2374 |
| cta gcc aga gcc tct ttg gct ctt cca act tcc tcc ctg tcc cgg acc Leu Ala Arg Ala Ser Leu Ala Leu Pro Thr Ser Ser Leu Ser Arg Thr 680 685 690 | 2422 |
| gcg tcc cag agc agc agt cac cga ggc tgg gag atc ctt cgt caa aac Ala Ser Gln Ser Ser His Arg Gly Trp Glu Ile Leu Arg Gln Asn 695 700 705 | 2470 |
| acc ctg ggg cac ttg aat ctt gga ctg aac ctt agt gag ggg gat gga Thr Leu Gly His Leu Asn Leu Gly Leu Asn Leu Ser Glu Gly Asp Gly 710 715 720 | 2518 |
| gag gag gtc tac cat ttt tgattaacat cgctatcact cttgacccta Glu Glu Val Tyr His Phe 725 | 2566 |
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| cttctgtgcc tgtaatcat gggagggtga gacagaacaa tccctaaagg gtcatgcctc | 2686 |
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| tgggcttttg caagtcaccc atctcaggaa aaaggaggtt ggcaactaaa gacatgaggc | 2806 |
| agggatgcta gattaatgtc aggacccatt tctctctgc cccacgcagc ccctagaaaag | 2866 |
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50 55 60

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Thr Ala Leu His Ile Ala Ala Leu Tyr Asp Asn Leu Glu Ala Ala Leu
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Val Leu Met Glu Ala Ala Pro Glu Leu Val Phe Glu Pro Thr Thr Cys
 100 105 110

Glu Ala Phe Ala Gly Gln Thr Ala Leu His Ile Ala Val Val Asn Gln
 115 120 125

Asn Val Asn Leu Val Arg Ala Leu Leu Thr Arg Arg Ala Ser Val Ser
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Ala Arg Ala Thr Gly Thr Ala Phe Arg Arg Ser Pro Arg Asn Leu Ile
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Tyr Phe Gly Glu His Pro Leu Ser Phe Ala Ala Cys Val Asn Ser Glu
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Glu Ile Val Arg Leu Leu Ile Glu His Gly Ala Asp Ile Arg Ala Gln
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Asp Ser Leu Gly Asn Thr Val Leu His Ile Leu Ile Leu Gln Pro Asn
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Lys Thr Phe Ala Cys Gln Met Tyr Asn Leu Leu Ser Tyr Asp Gly
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His Gly Asp His Leu Gln Pro Leu Asp Leu Val Pro Asn His Gln Gly
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Leu Thr Pro Phe Lys Leu Ala Gly Val Glu Gly Asn Thr Val Met Phe
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Trp Asn Lys Tyr Gly Arg Pro Tyr Phe Cys Ile Leu Ala Ala Leu Tyr
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Lys Phe Arg Gly Gly Asn Arg Thr His Ser Arg Asp Ile Thr Ile Leu
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Gln Gln Lys Leu Leu Gln Glu Ala Tyr Glu Thr Arg Glu Asp Ile Ile
 370 375 380

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Gly Lys Thr Ile Leu Gly Gly Pro Phe His Val Ile Ile Ile Thr Tyr
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Ala Ser Leu Val Leu Val Thr Met Val Met Arg Leu Thr Asn Thr Asn
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Gly Glu Val Val Pro Met Ser Phe Ala Leu Val Leu Gly Trp Cys Ser
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Gln Thr Glu Asp Pro Thr Ser Leu Gly Gln Phe Tyr Asp Tyr Pro Met
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Pro Leu Arg Val Leu Arg Tyr Val Glu Val Phe Lys Asn Ser Asp Lys
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Glu Asp Asp Gln Glu His Pro Ser Glu Lys Gln Pro Ser Gly Ala Glu
 660 665 670

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| gccgtgggc atg ggc ctg gta cgc agc gtg ggc gcc ttg gcc gtg gtg gcc | 171 |
| Met Gly Leu Val Arg Ser Val Gly Ala Leu Ala Val Val Ala | |
| 1 5 10 | |
| gcc att ttt ggc ctg gag ttc ctc atg gtg tcc cag ttg tgc gag gac | 219 |
| Ala Ile Phe Gly Leu Glu Phe Leu Met Val Ser Gln Leu Cys Glu Asp | |
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| aaa cac tca cag tgc aag tgg gtc atg ggt tcc atc ctc ctc ctg gtg | 267 |
| Lys His Ser Gln Cys Lys Trp Val Met Gly Ser Ile Leu Leu Leu Val | |
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| tct ttc gtc ctc tcc tcc ggc ggg ctc ctg ggt ttt gtg atc ctc ctc | 315 |
| Ser Phe Val Leu Ser Ser Gly Gly Leu Leu Gly Phe Val Ile Leu Leu | |
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| agg aac caa gtc aca ctc atc ggc ttc acc cta atg ttt tgg tgc gaa | 363 |
| Arg Asn Gln Val Thr Leu Ile Gly Phe Thr Leu Met Phe Trp Cys Glu | |
| 65 70 75 | |
| ttc act gcc tcc ttc ctc ttc ctg aac gcc atc agc ggc ctt cac | 411 |
| Phe Thr Ala Ser Phe Leu Leu Phe Leu Asn Ala Ile Ser Gly Leu His | |
| 80 85 90 | |
| atc aac agc atc acc cat ccc tgg gaa tgaccgtgga aatttttaggc | 458 |
| Ile Asn Ser Ile Thr His Pro Trp Glu | |
| 95 100 | |
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| gtggccctcg gtggggctgg gtggacaag ggccctgaaa cggctgcctg tttgccata | 578 |
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cccaaggccc gtgtgtcat gtgtctgtct ttgtgaggg ttagacagcc tcagggcacc 1298
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Val Leu Ser Ser Gly Gly Leu Leu Gly Phe Val Ile Leu Leu Arg Asn
 50 55 60

Gln Val Thr Leu Ile Gly Phe Thr Leu Met Phe Trp Cys Glu Phe Thr
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| <210> 144 | |
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160 200 PCT FINAL.ST25

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tta act gaa caa gca gag ctt cag ctg ccc ctc ttc tgc ctc ttc tta
Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu
20 25 30

96

gga att tac aca gtt act gtg gtg gga aac ctc agc atg atc tca att
Gly Ile Tyr Thr Val Thr Val Gly Asn Leu Ser Met Ile Ser Ile
35 40 45

144

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Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser
50 55 60

192

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Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys
65 70 75 80

240

atg cta tca ggg ttt tta tgc aga gat aga tcc atc tcc tat tct gga
Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly
85 90 95

288

tgc atg att cag ctg ttt ttc tgt gtt tgt att tct gaa tgc
Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys
100 105 110

336

tat atg ctg gca gcc atg gcc tgc gat cgc tac gtg gcc atc tgc agc
Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser
115 120 125

384

cca ctg ctc tac agg gtc atc atg tcc cct agg gtc tgt tct ctg ctg
Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu
130 135 140

432

gtg gct gtc ttc tca gta ggt ttc act gat gct gtg atc cat gga
Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly
145 150 155 160

480

ggc tgt ata ctc agg ttg tct ttc tgt gga tca aac atc att aaa cat
Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His
165 170 175

528

tat ttc tgt gac att gtc cct ctt att aaa ctc tcc tgc tcc agc act
Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr
180 185 190

576

tat att gat gag ctt ttg att ttt gtc att ggt gga ttt aac atg gtg
Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val
195 200 205

624

gcc aca agc cta aca atc att att tca tat gct ttt atc ctc acc agc
Ala Thr Ser Leu Thr Ile Ile Ser Tyr Ala Phe Ile Leu Thr Ser
210 215 220

672

atc ctg cgc atc cac tct aaa aag ggc agg tgc aaa gcg ttt agc acc
Ile Leu Arg Ile His Ser Lys Lys Gly Arg Cys Lys Ala Phe Ser Thr
225 230 235 240

720

tgt agc tcc cac ctg aca gct gtt ctt atg ttt tat ggg tct ctg atg

768

16U 200 PCT FINAL.ST25

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|-------------------------|-----|-----|---|--|-----|---|--|-----|-----|-----|-----------|---|--|-----------|---|--|-----------|-----|-----|--------------------|---|--|-----------|---|--|---|-----|-----|--------------------|---|----|-----------|---|--|---|-----|----|--------------------|----|----|---|---|--|---|----|----|--------------------|----|---|---|---|--|---|----|----|----|---|---|---|---|----|----|----|----|---|---|---|---|----|----|----|----|---|---|---|---|-----|-----|-----|----|---|---|---|---|-----|-----|-----|-----|---|---|---|---|-----|-----|-----|-----|---|---|---|---|-----|-----|-----|-----|---|---|---|---|-----|-----|-----|-----|---|---|---|---|-----|-----|-----|-----|---|---|---|---|-----|-----|-----|-----|-----|---|---|---|--|-----|-----|-----|-----|-----|---|---|--|--|-----|-----|-----|-----|--|---|--|--|--|-----|-----|-----|--|
| Cys Ser Ser His Leu Thr Ala Val Leu Met | Phe Tyr Gly Ser Leu Met | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 245 | 250 | 255 | | tcc atg tat ctc aaa cct gct tct agc agt tca ctc acc cag gag aaa | | 816 | Ser Met Tyr Leu Lys Pro Ala Ser Ser Ser Leu Thr Gln Glu Lys | | 260 | 265 | 270 | | gta tcc tca gta ttt tat acc act gtg att ctc atg ttg aat ccc ttg | | 864 | Val Ser Ser Val Phe Tyr Thr Val Ile Leu Met Leu Asn Pro Leu | | 275 | 280 | 285 | | ata tat agt ctg agg aac aat gaa gta aga aat gct ctg atg aaa ctt | | 912 | Ile Tyr Ser Leu Arg Asn Asn Glu Val Arg Asn Ala Leu Met Lys Leu | | 290 | 295 | 300 | | tta aga aga aaa ata tct tta tct cca gga taa | | 945 | Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly | | 305 | 310 | | <210> 153 | | | <211> 314 | | | <212> PRT | | | <213> Homo sapiens | | | <400> 153 | | | Met Gly Val Lys Asn His Ser Thr Val Thr Glu Phe Leu Leu Ser Gly | | | 1 | 5 | 10 | 15 | Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu | | | | 20 | 25 | 30 | | Gly Ile Tyr Thr Val Thr Val Val Gly Asn Leu Ser Met Ile Ser Ile | | | | 35 | 40 | 45 | | Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser | | | | 50 | 55 | 60 | | Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys | | | | 65 | 70 | 75 | 80 | Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly | | | | 85 | 90 | 95 | | Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys | | | | 100 | 105 | 110 | | Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser | | | | 115 | 120 | 125 | | Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu | | | | 130 | 135 | 140 | | Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly | | | | 145 | 150 | 155 | 160 | Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His | | | | 165 | 170 | 175 | | Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr | | | | 180 | 185 | 190 | | Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val | | | | 195 | 200 | 205 | |
| 255 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| tcc atg tat ctc aaa cct gct tct agc agt tca ctc acc cag gag aaa | | 816 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ser Met Tyr Leu Lys Pro Ala Ser Ser Ser Leu Thr Gln Glu Lys | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 260 | 265 | 270 | | gta tcc tca gta ttt tat acc act gtg att ctc atg ttg aat ccc ttg | | 864 | Val Ser Ser Val Phe Tyr Thr Val Ile Leu Met Leu Asn Pro Leu | | 275 | 280 | 285 | | ata tat agt ctg agg aac aat gaa gta aga aat gct ctg atg aaa ctt | | 912 | Ile Tyr Ser Leu Arg Asn Asn Glu Val Arg Asn Ala Leu Met Lys Leu | | 290 | 295 | 300 | | tta aga aga aaa ata tct tta tct cca gga taa | | 945 | Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly | | 305 | 310 | | <210> 153 | | | <211> 314 | | | <212> PRT | | | <213> Homo sapiens | | | <400> 153 | | | Met Gly Val Lys Asn His Ser Thr Val Thr Glu Phe Leu Leu Ser Gly | | | 1 | 5 | 10 | 15 | Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu | | | | 20 | 25 | 30 | | Gly Ile Tyr Thr Val Thr Val Val Gly Asn Leu Ser Met Ile Ser Ile | | | | 35 | 40 | 45 | | Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser | | | | 50 | 55 | 60 | | Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys | | | | 65 | 70 | 75 | 80 | Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly | | | | 85 | 90 | 95 | | Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys | | | | 100 | 105 | 110 | | Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser | | | | 115 | 120 | 125 | | Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu | | | | 130 | 135 | 140 | | Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly | | | | 145 | 150 | 155 | 160 | Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His | | | | 165 | 170 | 175 | | Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr | | | | 180 | 185 | 190 | | Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val | | | | 195 | 200 | 205 | | | | | | | | | | |
| 270 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| gta tcc tca gta ttt tat acc act gtg att ctc atg ttg aat ccc ttg | | 864 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Val Ser Ser Val Phe Tyr Thr Val Ile Leu Met Leu Asn Pro Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 275 | 280 | 285 | | ata tat agt ctg agg aac aat gaa gta aga aat gct ctg atg aaa ctt | | 912 | Ile Tyr Ser Leu Arg Asn Asn Glu Val Arg Asn Ala Leu Met Lys Leu | | 290 | 295 | 300 | | tta aga aga aaa ata tct tta tct cca gga taa | | 945 | Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly | | 305 | 310 | | <210> 153 | | | <211> 314 | | | <212> PRT | | | <213> Homo sapiens | | | <400> 153 | | | Met Gly Val Lys Asn His Ser Thr Val Thr Glu Phe Leu Leu Ser Gly | | | 1 | 5 | 10 | 15 | Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu | | | | 20 | 25 | 30 | | Gly Ile Tyr Thr Val Thr Val Val Gly Asn Leu Ser Met Ile Ser Ile | | | | 35 | 40 | 45 | | Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser | | | | 50 | 55 | 60 | | Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys | | | | 65 | 70 | 75 | 80 | Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly | | | | 85 | 90 | 95 | | Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys | | | | 100 | 105 | 110 | | Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser | | | | 115 | 120 | 125 | | Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu | | | | 130 | 135 | 140 | | Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly | | | | 145 | 150 | 155 | 160 | Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His | | | | 165 | 170 | 175 | | Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr | | | | 180 | 185 | 190 | | Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val | | | | 195 | 200 | 205 | | | | | | | | | | | | | | | | | | | |
| 285 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ata tat agt ctg agg aac aat gaa gta aga aat gct ctg atg aaa ctt | | 912 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ile Tyr Ser Leu Arg Asn Asn Glu Val Arg Asn Ala Leu Met Lys Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 290 | 295 | 300 | | tta aga aga aaa ata tct tta tct cca gga taa | | 945 | Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly | | 305 | 310 | | <210> 153 | | | <211> 314 | | | <212> PRT | | | <213> Homo sapiens | | | <400> 153 | | | Met Gly Val Lys Asn His Ser Thr Val Thr Glu Phe Leu Leu Ser Gly | | | 1 | 5 | 10 | 15 | Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu | | | | 20 | 25 | 30 | | Gly Ile Tyr Thr Val Thr Val Val Gly Asn Leu Ser Met Ile Ser Ile | | | | 35 | 40 | 45 | | Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser | | | | 50 | 55 | 60 | | Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys | | | | 65 | 70 | 75 | 80 | Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly | | | | 85 | 90 | 95 | | Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys | | | | 100 | 105 | 110 | | Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser | | | | 115 | 120 | 125 | | Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu | | | | 130 | 135 | 140 | | Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly | | | | 145 | 150 | 155 | 160 | Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His | | | | 165 | 170 | 175 | | Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr | | | | 180 | 185 | 190 | | Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val | | | | 195 | 200 | 205 | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 300 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| tta aga aga aaa ata tct tta tct cca gga taa | | 945 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 305 | 310 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <210> 153 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <211> 314 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <212> PRT | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <213> Homo sapiens | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <400> 153 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Met Gly Val Lys Asn His Ser Thr Val Thr Glu Phe Leu Leu Ser Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | 5 | 10 | 15 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Thr Glu Gln Ala Glu Leu Gln Leu Pro Leu Phe Cys Leu Phe Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 20 | 25 | 30 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gly Ile Tyr Thr Val Thr Val Val Gly Asn Leu Ser Met Ile Ser Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 35 | 40 | 45 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ile Arg Leu Asn Arg Gln Leu His Thr Pro Met Tyr Tyr Phe Leu Ser | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 50 | 55 | 60 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ser Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Val Ile Thr Pro Lys | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 65 | 70 | 75 | 80 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Met Leu Ser Gly Phe Leu Cys Arg Asp Arg Ser Ile Ser Tyr Ser Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 85 | 90 | 95 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Cys Met Ile Gln Leu Phe Phe Cys Val Cys Val Ile Ser Glu Cys | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 100 | 105 | 110 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tyr Met Leu Ala Ala Met Ala Cys Asp Arg Tyr Val Ala Ile Cys Ser | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 115 | 120 | 125 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pro Leu Leu Tyr Arg Val Ile Met Ser Pro Arg Val Cys Ser Leu Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 130 | 135 | 140 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Val Ala Ala Val Phe Ser Val Gly Phe Thr Asp Ala Val Ile His Gly | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 145 | 150 | 155 | 160 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gly Cys Ile Leu Arg Leu Ser Phe Cys Gly Ser Asn Ile Ile Lys His | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 165 | 170 | 175 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tyr Phe Cys Asp Ile Val Pro Leu Ile Lys Leu Ser Cys Ser Ser Thr | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 180 | 185 | 190 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tyr Ile Asp Glu Leu Leu Ile Phe Val Ile Gly Gly Phe Asn Met Val | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 195 | 200 | 205 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

16U 200 PCT FINAL.ST25
 Ala Thr Ser Leu Thr Ile Ile Ser Tyr Ala Phe Ile Leu Thr Ser
 210 215 220

Ile Leu Arg Ile His Ser Lys Lys Gly Arg Cys Lys Ala Phe Ser Thr
 225 230 235 240

Cys Ser Ser His Leu Thr Ala Val Leu Met Phe Tyr Gly Ser Leu Met
 245 250 255

Ser Met Tyr Leu Lys Pro Ala Ser Ser Ser Leu Thr Gln Glu Lys
 260 265 270

Val Ser Ser Val Phe Tyr Thr Val Ile Leu Met Leu Asn Pro Leu
 275 280 285

Ile Tyr Ser Leu Arg Asn Asn Glu Val Arg Asn Ala Leu Met Lys Leu
 290 295 300

Leu Arg Arg Lys Ile Ser Leu Ser Pro Gly
 305 310

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| <210> 161 | |
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| <210> 162 | |
| <211> 957 | |
| <212> DNA | |
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| Met Asn Pro Ala Asn His Ser Gln Val Ala Gly Phe Val Leu Leu Gly | |
| 1 5 10 15 | |
| ctc tct cag gtt tgg gag ctt cgg ttt gtt ttc ttc act gtt ttc tct | 96 |
| Leu Ser Gln Val Trp Glu Leu Arg Phe Val Phe Phe Thr Val Phe Ser | |
| 20 25 30 | |
| gct gtg tat ttt atg act gta gtg gga aac ctt ctt att gtg gtc ata | 144 |
| Ala Val Tyr Phe Met Thr Val Val Gly Asn Leu Ile Val Val Ile | |
| 35 40 45 | |
| gtg acc tcc gac cca cac ctg cac aca acc atg tat ttt ctc ttg ggc | 192 |
| Val Thr Ser Asp Pro His Leu His Thr Met Tyr Phe Leu Leu Gly | |
| 50 55 60 | |
| aat ctt tct ttc ctg gac ttt tgc tac tct tcc atc aca gca cct agg | 240 |
| Asn Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Ile Thr Ala Pro Arg | |
| 65 70 75 80 | |
| atg ctg gtt gac ttg ctc tca ggc aac cct acc att tcc ttt ggt gga | 288 |
| Met Leu Val Asp Leu Ser Gly Asn Pro Thr Ile Ser Phe Gly Gly | |
| 85 90 95 | |
| tgc ctg actcaa ctc ttc ttc cac ttc att gga ggc atc aag atc | 336 |
| Cys Leu Thr Gln Leu Phe Phe His Phe Ile Gly Gly Ile Lys Ile | |
| 100 105 110 | |
| ttc ctg ctg act gtc atg gcg tat gac cgc tac att gcc att tcc cag | 384 |
| Phe Leu Leu Thr Val Met Ala Tyr Asp Arg Tyr Ile Ala Ile Ser Gln | |
| 115 120 125 | |
| ccc ctg cac tac acg ctc att atg aat cag act gtc tgt gca ctc ctt | 432 |
| Pro Leu His Tyr Thr Leu Ile Met Asn Gln Thr Val Cys Ala Leu Leu | |
| 130 135 140 | |
| atg gca gcc tcc tgg gtg ggg ggc ttc atc cac tcc ata gta cag att | 480 |
| Met Ala Ala Ser Trp Val Gly Gly Phe Ile His Ser Ile Val Gln Ile | |
| 145 150 155 160 | |
| gca ttg act atc cag ctg cca ttc tgt ggg cct gac aag ctg gac aac | 528 |
| Ala Leu Thr Ile Gln Leu Pro Phe Cys Gly Pro Asp Lys Leu Asp Asn | |
| 165 170 175 | |
| ttt tat tgt gat gtg cct cag ctg atc aaa ttg gcc tgc aca gat acc | 576 |
| Phe Tyr Cys Asp Val Pro Gln Leu Ile Lys Leu Ala Cys Thr Asp Thr | |
| 180 185 190 | |

16U 200 PCT FINAL.ST25

ttt gtc tta gag ctt tta atg gtg tct aac aat ggc ctg gtg acc ctg
 Phe Val Leu Glu Leu Leu Met Val Ser Asn Asn Gly Leu Val Thr Leu
 195 200 205

atg tgt ttt ctg gtg ctt ctg gga tcg tac aca gca ctg cta gtc atg
 Met Cys Phe Leu Val Leu Leu Gly Ser Tyr Thr Ala Leu Leu Val Met
 210 215 220

ctc cga agc cac tca cgg gag ggc cgc agc aag gcc ctg tct acc tgt
 Leu Arg Ser His Ser Arg Glu Gly Arg Ser Lys Ala Leu Ser Thr Cys
 225 230 235 240

gcc tct cac att gct gtg gtg acc tta atc ttt gtg cct tgc atc tac
 Ala Ser His Ile Ala Val Val Thr Leu Ile Phe Val Pro Cys Ile Tyr
 245 250 255

gtc tat aca agg cct ttt cgg aca ttc ccc atg gac aag gcc gtc tct
 Val Tyr Thr Arg Pro Phe Arg Thr Phe Pro Met Asp Lys Ala Val Ser
 260 265 270

gtg cta tac aca att gtc acc ccc atg ctg aat cct gcc atc tat acc
 Val Leu Tyr Thr Ile Val Thr Pro Met Leu Asn Pro Ala Ile Tyr Thr
 275 280 285

ctg aga aac aag gaa gtg atc atg gcc atg aag aag ctg tgg agg agg
 Leu Arg Asn Lys Glu Val Ile Met Ala Met Lys Lys Leu Trp Arg Arg
 290 295 300

aaa aag gac cct att ggt ccc ctg gag cac aga ccc tta cat tag
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Leu Ser Gln Val Trp Glu Leu Arg Phe Val Phe Phe Thr Val Phe Ser
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Ala Val Tyr Phe Met Thr Val Val Gly Asn Leu Leu Ile Val Val Ile
 35 40 45

Val Thr Ser Asp Pro His Leu His Thr Thr Met Tyr Phe Leu Leu Gly
 50 55 60

Asn Leu Ser Phe Leu Asp Phe Cys Tyr Ser Ser Ile Thr Ala Pro Arg
 65 70 75 80

Met Leu Val Asp Leu Leu Ser Gly Asn Pro Thr Ile Ser Phe Gly Gly
 85 90 95

Cys Leu Thr Gln Leu Phe Phe His Phe Ile Gly Gly Ile Lys Ile
 100 105 110

Phe Leu Leu Thr Val Met Ala Tyr Asp Arg Tyr Ile Ala Ile Ser Gln
 115 120 125

Pro Leu His Tyr Thr Leu Ile Met Asn Gln Thr Val Cys Ala Leu Leu
 130 135 140

Met Ala Ala Ser Trp Val Gly Gly Phe Ile His Ser Ile Val Gln Ile
 145 150 155 160

16U 200 PCT FINAL.ST25

Ala Leu Thr Ile Gln Leu Pro Phe Cys Gly Pro Asp Lys Leu Asp Asn
 165 170 175

Phe Tyr Cys Asp Val Pro Gln Leu Ile Lys Leu Ala Cys Thr Asp Thr
 180 185 190

Phe Val Leu Glu Leu Leu Met Val Ser Asn Asn Gly Leu Val Thr Leu
 195 200 205

Met Cys Phe Leu Val Leu Leu Gly Ser Tyr Thr Ala Leu Leu Val Met
 210 215 220

Leu Arg Ser His Ser Arg Glu Gly Arg Ser Lys Ala Leu Ser Thr Cys
 225 230 235 240

Ala Ser His Ile Ala Val Val Thr Leu Ile Phe Val Pro Cys Ile Tyr
 245 250 255

Val Tyr Thr Arg Pro Phe Arg Thr Phe Pro Met Asp Lys Ala Val Ser
 260 265 270

Val Leu Tyr Thr Ile Val Thr Pro Met Leu Asn Pro Ala Ile Tyr Thr
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Lys Lys Asp Pro Ile Gly Pro Leu Glu His Arg Pro Leu His
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tcc ccc agt agc cac ctc ata cag ttc ctg gtg ttc ctg ggg tta atg 96
Phe Pro Ser Ser His Leu Ile Gln Phe Leu Val Phe Leu Gly Leu Met
20 25 30

gtg acc tac att gta aca gcc aca ggc aag ctg cta att att gtg ctc 144
Val Thr Tyr Ile Val Thr Ala Thr Gly Lys Leu Leu Ile Val Leu
35 40 45

agc tgg ata gac caa cgc ctg cac ata cag atg tac ttc ttc ctg cgg 192
Ser Trp Ile Asp Gln Arg Leu His Ile Gln Met Tyr Phe Phe Leu Arg
50 55 60

aat ttc tcc ttc ctg gag ctg ttg ctg gta act gtt gtg gtt ccc aag 240
Asn Phe Ser Phe Leu Glu Leu Leu Val Thr Val Val Val Pro Lys
65 70 75 80

atg ctt gtc gtc atc ctc acg ggg gat cac acc atc tca ttt gtc agc 288
Met Leu Val Val Ile Leu Thr Gly Asp His Thr Ile Ser Phe Val Ser
85 90 95

tgc atc atc cag tcc tac ctc tac ttc ttt cta ggc acc act gac ttc 336
Cys Ile Ile Gln Ser Tyr Leu Tyr Phe Phe Leu Gly Thr Thr Asp Phe
100 105 110

ttc ctc ttg gcc gtc atg tct ctg gat cgt tac ctg gca atc tgc cga 384
Phe Leu Leu Ala Val Met Ser Leu Asp Arg Tyr Leu Ala Ile Cys Arg
115 120 125

cca ctc cgc tat gag acc ctg atg aat ggc cat gtc tgt tcc caa cta 432
Pro Leu Arg Tyr Glu Thr Leu Met Asn Gly His Val Cys Ser Gln Leu
130 135 140

gtg ctg gcc tcc tgg cta gct gga ttc ctc tgg gtc ctt tgc ccc act 480
Val Leu Ala Ser Trp Leu Ala Gly Phe Leu Trp Val Leu Cys Pro Thr
145 150 155 160

gtc ctc atg gcc agc ctg cct ttc tgt ggc ccc aat ggt att gac cac 528
Val Leu Met Ala Ser Leu Pro Phe Cys Gly Pro Asn Gly Ile Asp His
165 170 175

ttc ttt cgt gac agt tgg ccc ttg ctc agg ctt tct tgt ggg gac acc 576
Phe Phe Arg Asp Ser Trp Pro Leu Leu Arg Leu Ser Cys Gly Asp Thr
180 185 190

cac ctg ctg aaa ctg qtg gct ttc atg ctc tct acg ttg qtg tta ctg 624
His Leu Leu Lys Leu Val Ala Phe Met Leu Ser Thr Leu Val Leu Leu
195 200 205

ggc tca ctg qct ctg acc tca gtt tcc tat gcc tgc att ctt gcc act 672
Gly Ser Leu Ala Leu Thr Ser Val Ser Tyr Ala Cys Ile Leu Ala Thr
210 215 220

gtt ctc agg gcc cct aca gct gct gag cga agg aaa gcg ttt tcc act 720
Val Leu Arg Ala Pro Thr Ala Ala Glu Arg Arg Lys Ala Phe Ser Thr
225 230 235 240

tgc gcc tcg cat ctt aca gtg gtg gtc atc atc tat ggc agt tcc atc 768
Cys Ala Ser His Leu Thr Val Val Ile Ife Ife Tyr Gly Ser Ser Ile
245 250 255

ttt ctc tac att cgt atg tca gag gct cag tcc aaa ctg ctc aac aaa 816
Phe Leu Tyr Ile Arg Met Ser Glu Ala Gln Ser Lys Leu Leu Asn Lys
260 265 270

ggt gcc tcc gtc ctg agc tgc atc atc aca ccc ctc ttg aac cca ttc 864
Gly Ala Ser Val Leu Ser Cys Ile Ile Thr Pro Leu Leu Asn Pro Phe
275 280 285

atc ttc act ctc cgc aat gac aag gtg cag caa gca ctg aga gaa gcc 912
Ile Phe Thr Leu Arg Asn Asp Lys Val Gln Gln Ala Leu Arg Glu Ala
290 295 300

ttg ggg tgg ccc agg ctc act gct gtg atg aaa ctg agg gtc aca agt 960
Leu Gly Trp Pro Arg Leu Thr Ala Val Met Lys Leu Arg Val Thr Ser

305 310 160 200 PCT FINAL.ST25
 315 320

caa agg aaa tga
 Gln Arg Lys

972

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 <212> PRT
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<400> 168

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Val Thr Tyr Ile Val Thr Ala Thr Gly Lys Leu Leu Ile Ile Val Leu
 35 40 45

Ser Trp Ile Asp Gln Arg Leu His Ile Gln Met Tyr Phe Phe Leu Arg
 50 55 60

Asn Phe Ser Phe Leu Glu Leu Leu Leu Val Thr Val Val Val Pro Lys
 65 70 75 80

Met Leu Val Val Ile Leu Thr Gly Asp His Thr Ile Ser Phe Val Ser
 85 90 95

Cys Ile Ile Gln Ser Tyr Leu Tyr Phe Phe Leu Gly Thr Thr Asp Phe
 100 105 110

Phe Leu Leu Ala Val Met Ser Leu Asp Arg Tyr Leu Ala Ile Cys Arg
 115 120 125

Pro Leu Arg Tyr Glu Thr Leu Met Asn Gly His Val Cys Ser Gln Leu
 130 135 140

Val Leu Ala Ser Trp Leu Ala Gly Phe Leu Trp Val Leu Cys Pro Thr
 145 150 155 160

Val Leu Met Ala Ser Leu Pro Phe Cys Gly Pro Asn Gly Ile Asp His
 165 170 175

Phe Phe Arg Asp Ser Trp Pro Leu Leu Arg Leu Ser Cys Gly Asp Thr
 180 185 190

His Leu Leu Lys Leu Val Ala Phe Met Leu Ser Thr Leu Val Leu Leu
 195 200 205

Gly Ser Leu Ala Leu Thr Ser Val Ser Tyr Ala Cys Ile Leu Ala Thr
 210 215 220

Val Leu Arg Ala Pro Thr Ala Ala Glu Arg Arg Lys Ala Phe Ser Thr
 225 230 235 240

Cys Ala Ser His Leu Thr Val Val Ile Ile Tyr Gly Ser Ser Ile
 245 250 255

Phe Leu Tyr Ile Arg Met Ser Glu Ala Gln Ser Lys Leu Leu Asn Lys

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260 265 270

Gly Ala Ser Val Leu Ser Cys Ile Ile Thr Pro Leu Leu Asn Pro Phe
275 280 285

Ile Phe Thr Leu Arg Asn Asp Lys Val Gln Gln Ala Leu Arg Glu Ala
290 295 300

Leu Gly Trp Pro Arg Leu Thr Ala Val Met Lys Leu Arg Val Thr Ser
305 310 315 320

Gln Arg Lys

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Met Asp Leu Pro His Val Pro Ala Leu Asp Ala Pro Leu Phe Gly Val
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ttc ctg gtg gtt tat gtg ctt act gtg ctg ggg aac ctc ctc atc ctg 96
Phe Leu Val Val Tyr Val Leu Thr Val Leu Gly Asn Leu Leu Ile Leu
20 25 30

ctg gtg atc agg gtg tac tct cac ctc cac acc ccc aag tac tac ttc 144
Leu Val Ile Arg Val Tyr Ser His Leu His Thr Pro Lys Tyr Tyr Phe
35 40 45

etc acc aat ctg tcc att gac ttg tgg ttc act gtc atg gtg 192
Leu Thr Asn Leu Ser Phe Ile Asp Leu Trp Phe Phe Thr Val Met Val
50 55 60

ccc aaa atg ccg agg acc ttg ttg tcc ctg tgt ggc aag gct gtg tcc 240
Pro Lys Met Pro Arg Thr Leu Leu Ser Leu Cys Gly Lys Ala Val Ser
65 70 75 80

ttc cac agt tgt atg acc caa ctc tat ttc ttc tac ttc ctg ggg agc 288
Phe His Ser Cys Met Thr Gln Leu Tyr Phe Phe Tyr Phe Leu Gly Ser
85 90 95

acc gag tgt ttg ctc tac acg gtc atg tcc tat gat cgc tat aga gga 336
Thr Glu Cys Leu Tyr Thr Val Met Ser Tyr Asp Arg Tyr Arg Gly
100 105 110

aat act cag cac ttc cca ggt agt gaa aac act ccc cac gaa gtg agc 384
Asn Thr Gln His Phe Pro Gly Ser Glu Asn Thr Pro His Glu Val Ser
115 120 125

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caa atg cta gtg gcc cgg ggg gca cac ggg ctc cca ctc atc atc ctg 432
 Gln Met Leu Val Ala Arg Gly Ala His Gly Leu Pro Leu Ile Ile Leu
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 Ala Asp Leu Ser Gly
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<210> 172
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 20 25 30

Leu Val Ile Arg Val Tyr Ser His Leu His Thr Pro Lys Tyr Tyr Phe
 35 40 45

Leu Thr Asn Leu Ser Phe Ile Asp Leu Trp Phe Phe Thr Val Met Val
 50 55 60

Pro Lys Met Pro Arg Thr Leu Leu Ser Leu Cys Gly Lys Ala Val Ser
 65 70 75 80

Phe His Ser Cys Met Thr Gln Leu Tyr Phe Phe Tyr Phe Leu Gly Ser
 85 90 95

Thr Glu Cys Leu Leu Tyr Thr Val Met Ser Tyr Asp Arg Tyr Arg Gly
 100 105 110

Asn Thr Gln His Phe Pro Gly Ser Glu Asn Thr Pro His Glu Val Ser
 115 120 125

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 130 135 140

Ala Asp Leu Ser Gly
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acccactcag atctgccagg atgatga 27

<210> 175
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| Met Ser Asn Ala Ser Leu Val Thr Ala Phe Ile Leu Thr Gly Leu Pro | | |
| 1 5 10 15 | | |
| cat gcc cca ggg ctg gac gcc ctc ctc ttt gga atc ttc ctg gtg gtt | 96 | |
| His Ala Pro Gly Leu Asp Ala Leu Leu Phe Gly Ile Phe Leu Val Val | | |
| 20 25 30 | | |
| tac gtg ctc act gtg ctg ggg aac ctc ctc atc ctg ctg gtg atc agg | 144 | |
| Tyr Val Leu Thr Val Leu Gly Asn Leu Leu Ile Leu Leu Val Ile Arg | | |
| 35 40 45 | | |
| gtg gat tct cac ctc cac acc ccc atg tac tac ttc ctc acc aac ctg | 192 | |
| Val Asp Ser His Leu His Thr Pro Met Tyr Tyr Phe Leu Thr Asn Leu | | |
| 50 55 60 | | |
| tcc ttc att gag atg tgg ttc tcc act gtc acg gtg ccc aaa atg ctg | 240 | |
| Ser Phe Ile Asp Met Trp Phe Ser Thr Val Thr Val Pro Lys Met Leu | | |
| 65 70 75 80 | | |
| atg acc ttg gtg tcc cca agc ggc agg gct atc tcc ttc cac agc tgc | 288 | |
| Met Thr Leu Val Ser Pro Ser Gly Arg Ala Ile Ser Phe His Ser Cys | | |
| 85 90 95 | | |
| gtg gct cag ctc tat ttt ttc cac ttc ctg ggg agc acc gag tgt ttc | 336 | |
| Val Ala Gln Leu Tyr Phe His Phe Leu Gly Ser Thr Glu Cys Phe | | |
| 100 105 110 | | |
| ctc tac aca gtc atg tcc tat gat cgc tac ttg gcc atc agt tac ccg | 384 | |
| Leu Tyr Thr Val Met Ser Tyr Asp Arg Tyr Leu Ala Ile Ser Tyr Pro | | |
| 115 120 125 | | |
| ctc agg tac acc agc atg atg agt ggg agc agg tgt gcc ctc ctg gcc | 432 | |
| Leu Arg Tyr Thr Ser Met Ser Gly Ser Arg Cys Ala Leu Leu Ala | | |
| 130 135 140 | | |
| acc ggc act ttg ctc agt ggc tct ctg cac tct gct gtc cag acc ata | 480 | |
| Thr Gly Thr Trp Leu Ser Gly Ser Leu His Ser Ala Val Gln Thr Ile | | |
| 145 150 155 160 | | |
| ttg act ttc cat ttg ccc tac tgt gga ccc aac cag atc cag cac tac | 528 | |
| Leu Thr Phe His Leu Pro Tyr Cys Gly Pro Asn Gln Ile Gln His Tyr | | |
| 165 170 175 | | |
| ttc tgt gac gca ccg ccc atc ctg aaa ctg gcc tgt gca gac acc tca | 576 | |
| Phe Cys Asp Ala Pro Pro Ile Leu Lys Leu Ala Cys Ala Asp Thr Ser | | |
| 180 185 190 | | |
| gcc aac gtg atg gtc atc ttt gtg gac att ggg ata gtg gcc tca ggc | 624 | |
| Ala Asn Val Met Val Ile Phe Val Asp Ile Gly Ile Val Ala Ser Gly | | |
| 195 200 205 | | |
| tgc ttt gtc ctg ata gtg ctg tcc tat gtg tcc atc gtc tgt tcc atc | 672 | |
| Cys Phe Val Leu Ile Val Leu Ser Tyr Val Ser Ile Val Cys Ser Ile | | |
| 210 215 220 | | |
| ctg cgg atc cgc acc tca gat ggg agg cgc aga gcc ttt cag acc tgt | 720 | |
| Leu Arg Ile Arg Thr Ser Asp Gly Arg Arg Ala Phe Gln Thr Cys | | |
| 225 230 235 240 | | |
| gcc tcc cac tgt att gtg gtc ctt tgc ttc ttt gtt ccc tgt gtt gtc | 768 | |
| Ala Ser His Cys Ile Val Val Leu Cys Phe Phe Val Pro Cys Val Val | | |
| 245 250 255 | | |
| att tat ctg agg cca ggc tcc atg gat gcc atg gat gga gtt gtg gcc | 816 | |
| Ile Tyr Leu Arg Pro Gly Ser Met Asp Ala Met Asp Gly Val Val Ala | | |
| 260 265 270 | | |
| att ttc tac act gtg ctg acg ccc ctt ctc aac cct gtt gtg tac acc | 864 | |
| Ile Phe Tyr Thr Val Leu Thr Pro Leu Leu Asn Pro Val Val Tyr Thr | | |
| 275 280 285 | | |

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|---|-----|
| ctg aga aac aag gag gtg aag aaa gct gtg ttg aaa ctt aga gac aaa | 912 |
| Leu Arg Asn Lys Glu Val Lys Lys Ala Val Leu Lys Leu Arg Asp Lys | |
| 290 | 295 |
| 295 | 300 |
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| gta gca cat cct cag agg aaa taa | 936 |
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| <212> PRT | |
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| Met Ser Asn Ala Ser Leu Val Thr Ala Phe Ile Leu Thr Gly Leu Pro | |
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| 5 | 10 |
| 10 | 15 |
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| His Ala Pro Gly Leu Asp Ala Leu Leu Phe Gly Ile Phe Leu Val Val | |
| 20 | 25 |
| 25 | 30 |
| | |
| Tyr Val Leu Thr Val Leu Gly Asn Leu Leu Ile Leu Leu Val Ile Arg | |
| 35 | 40 |
| 40 | 45 |
| | |
| Val Asp Ser His Leu His Thr Pro Met Tyr Tyr Phe Leu Thr Asn Leu | |
| 50 | 55 |
| 55 | 60 |
| | |
| Ser Phe Ile Asp Met Trp Phe Ser Thr Val Thr Val Pro Lys Met Leu | |
| 65 | 70 |
| 70 | 75 |
| 75 | 80 |
| | |
| Met Thr Leu Val Ser Pro Ser Gly Arg Ala Ile Ser Phe His Ser Cys | |
| 85 | 90 |
| 90 | 95 |
| | |
| Val Ala Gln Leu Tyr Phe Phe His Phe Leu Gly Ser Thr Glu Cys Phe | |
| 100 | 105 |
| 105 | 110 |
| | |
| Leu Tyr Thr Val Met Ser Tyr Asp Arg Tyr Leu Ala Ile Ser Tyr Pro | |
| 115 | 120 |
| 120 | 125 |
| | |
| Leu Arg Tyr Thr Ser Met Met Ser Gly Ser Arg Cys Ala Leu Leu Ala | |
| 130 | 135 |
| 135 | 140 |
| | |
| Thr Gly Thr Trp Leu Ser Gly Ser Leu His Ser Ala Val Gln Thr Ile | |
| 145 | 150 |
| 150 | 155 |
| 155 | 160 |
| | |
| Leu Thr Phe His Leu Pro Tyr Cys Gly Pro Asn Gln Ile Gln His Tyr | |
| 165 | 170 |
| 170 | 175 |
| 175 | |
| | |
| Phe Cys Asp Ala Pro Pro Ile Leu Lys Leu Ala Cys Ala Asp Thr Ser | |
| 180 | 185 |
| 185 | 190 |
| 190 | |
| | |
| Ala Asn Val Met Val Ile Phe Val Asp Ile Gly Ile Val Ala Ser Gly | |
| 195 | 200 |
| 200 | 205 |
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| | |
| Cys Phe Val Leu Ile Val Leu Ser Tyr Val Ser Ile Val Cys Ser Ile | |
| 210 | 215 |
| 215 | 220 |
| 220 | |
| | |
| Leu Arg Ile Arg Thr Ser Asp Gly Arg Arg Ala Phe Gln Thr Cys | |
| 225 | 230 |
| 230 | 235 |
| 235 | 240 |
| 240 | |
| | |
| Ala Ser His Cys Ile Val Val Leu Cys Phe Phe Val Pro Cys Val Val | |
| 245 | 250 |
| 250 | 255 |
| 255 | |

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Ile Tyr Leu Arg Pro Gly Ser Met Asp Ala Met Asp Gly Val Val Ala
 260 265 270

Ile Phe Tyr Thr Val Leu Thr Pro Leu Leu Asn Pro Val Val Tyr Thr
 275 280 285

Leu Arg Asn Lys Glu Val Lys Lys Ala Val Leu Lys Leu Arg Asp Lys
 290 295 300

Val Ala His Pro Gln Arg Lys
 305 310

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ttatttcctc tgaggatgtg ctactttgtc tct 33

<210> 179
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gctgggtgct ctttatatcc ccagagggag agagaccaag ggtgagaaga 50

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Met Val Thr Glu Leu Leu Leu Gly Phe Ser His Leu Ala Asp Leu
1 5 10 15 48

cag ggc ttg ctc ttc tct gtc ttt ctc act atc tac ctg ctg acc gtg
Gln Gly Leu Leu Phe Ser Val Phe Leu Thr Ile Tyr Leu Leu Thr Val
20 25 30 96

gca ggc aat ttc ctc att gtg gtc tcc act gat gct gcc ctc
Ala Gly Asn Phe Leu Ile Val Val Leu Val Ser Thr Asp Ala Ala Leu
35 40 45 144

cag tcc cct atg tac ttc ttc ctg cgc acc ctc tcg gcc ttg gag att
Gln Ser Pro Met Tyr Phe Phe Leu Arg Thr Leu Ser Ala Leu Glu Ile
50 55 60 192

16U 200 PCT FINAL.ST25

ggc tat acg tct gtc acg gtc ccc ctg cta ctt cac cac ctc ctt act
Gly Tyr Thr Ser Val Thr Val Pro Leu Leu Leu His His Leu Leu Thr
65 70 75 80

240

ggc cgg cgc cac atc tct cgc tct gga tgt gct ctc cag atg ttc ttc
Gly Arg Arg His Ile Ser Arg Ser Gly Cys Ala Leu Gln Met Phe Phe
85 90 95

288

tcc ctc ttc ttt ggc gcc acg gag tgc tgc ctc ctg gca gcc atg gcc
Phe Leu Phe Phe Gly Ala Thr Glu Cys Cys Leu Leu Ala Ala Met Ala
100 105 110

336

tat gac cgc tat gca gcc atc tgt gaa ccc ctc cgc tac cca ctg ctg
Tyr Asp Arg Tyr Ala Ala Ile Cys Glu Pro Leu Arg Tyr Pro Leu Leu
115 120 125

384

ctg agc cac cgg gtg tgt cta cag cta gct ggg tcg gcg tgg gcc tgt
Leu Ser His Arg Val Cys Leu Gln Leu Ala Gly Ser Ala Trp Ala Cys
130 135 140

432

ggg gtg ctg gtg ggg ctg ggc cac acc cct ttc atc ttc tct ttg ccc
Gly Val Leu Val Gly Leu Gly His Thr Pro Phe Ile Phe Ser Leu Pro
145 150 155 160

480

tcc tgc gcc ccc aat acc atc ccg cag ttc ttc tgt gag atc cag cct
Phe Cys Gly Pro Asn Thr Ile Pro Gln Phe Phe Cys Glu Ile Gln Pro
165 170 175

528

gtc ctg cag ctg gta tgt gga gac acc tcg ctt aat gaa ctg cag att
Val Leu Gln Leu Val Cys Gly Asp Thr Ser Leu Asn Glu Leu Gln Ile
180 185 190

576

atc ctg gca aca gcc ctc ctc atc ctc tgc ccc ttt ggc ctc atc ctg
Ile Leu Ala Thr Ala Leu Leu Ile Leu Cys Pro Phe Gly Leu Ile Leu
195 200 205

624

ggc tcc tac ggg cgt atc ctc gtt acc atc ttc cgg atc cca tct gtt
Gly Ser Tyr Gly Arg Ile Leu Val Thr Ile Phe Arg Ile Pro Ser Val
210 215 220

672

gcf ggc cgc aag gcc ttc tcc acc tgc tcc tcc cac ctg atc gtg
Ala Gly Arg Arg Lys Ala Phe Ser Thr Cys Ser Ser His Leu Ile Val
225 230 235 240

720

gtc tcc ctc ttc tat ggc acc gca ctc ttt atc tat att cgc cct aag
Val Ser Leu Phe Tyr Gly Thr Ala Leu Phe Ile Tyr Ile Arg Pro Lys
245 250 255

768

gcc agc tac gat ccg gcc act gac cct ctg gtg tcc ctc ttc tat gct
Ala Ser Tyr Asp Pro Ala Thr Asp Pro Leu Val Ser Leu Phe Tyr Ala
260 265 270

816

gtg gtc acc ccc atc ctc aac ccc atc atc tac agc ctg cgg aac aca
Val Val Thr Pro Ile Leu Asn Pro Ile Ile Tyr Ser Leu Arg Asn Thr
275 280 285

864

gag gtc aaa gct gcc cta aag aga acc atc cag aaa acg gtg cct atg
Glu Val Lys Ala Ala Leu Lys Arg Thr Ile Gln Lys Thr Val Pro Met
290 295 300

912

gag att tga
Glu Ile
305

921

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Met Val Thr Glu Phe Leu Leu Gly Phe Ser His Leu Ala Asp Leu
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Gln Gly Leu Leu Phe Ser Val Phe Leu Thr Ile Tyr Leu Leu Thr Val
20 25 30

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Ala Gly Asn Phe Leu Ile Val Val Leu Val Ser Thr Asp Ala Ala Leu
 35 40 45

Gln Ser Pro Met Tyr Phe Phe Leu Arg Thr Leu Ser Ala Leu Glu Ile
 50 55 60

Gly Tyr Thr Ser Val Thr Val Pro Leu Leu Leu His His Leu Leu Thr
 65 70 75 80

Gly Arg Arg His Ile Ser Arg Ser Gly Cys Ala Leu Gln Met Phe Phe
 85 90 95

Phe Leu Phe Phe Gly Ala Thr Glu Cys Cys Leu Leu Ala Ala Met Ala
 100 105 110

Tyr Asp Arg Tyr Ala Ala Ile Cys Glu Pro Leu Arg Tyr Pro Leu Leu
 115 120 125

Leu Ser His Arg Val Cys Leu Gln Leu Ala Gly Ser Ala Trp Ala Cys
 130 135 140

Gly Val Leu Val Gly Leu Gly His Thr Pro Phe Ile Phe Ser Leu Pro
 145 150 155 160

Phe Cys Gly Pro Asn Thr Ile Pro Gln Phe Phe Cys Glu Ile Gln Pro
 165 170 175

Val Leu Gln Leu Val Cys Gly Asp Thr Ser Leu Asn Glu Leu Gln Ile
 180 185 190

Ile Leu Ala Thr Ala Leu Leu Ile Leu Cys Pro Phe Gly Leu Ile Leu
 195 200 205

Gly Ser Tyr Gly Arg Ile Leu Val Thr Ile Phe Arg Ile Pro Ser Val
 210 215 220

Ala Gly Arg Arg Lys Ala Phe Ser Thr Cys Ser Ser His Leu Ile Val
 225 230 235 240

Val Ser Leu Phe Tyr Gly Thr Ala Leu Phe Ile Tyr Ile Arg Pro Lys
 245 250 255

Ala Ser Tyr Asp Pro Ala Thr Asp Pro Leu Val Ser Leu Phe Tyr Ala
 260 265 270

Val Val Thr Pro Ile Leu Asn Pro Ile Ile Tyr Ser Leu Arg Asn Thr
 275 280 285

Glu Val Lys Ala Ala Leu Lys Arg Thr Ile Gln Lys Thr Val Pro Met
 290 295 300

Glu Ile
 305

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16U 200 PCT FINAL.ST25

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ctcggttct cccacctggc 20

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ggcgccaaag aagaggaaga aga 23

<210> 185
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Met Gly Arg Gly Asn Ser Thr Glu Val Thr Glu Phe His Leu Leu Gly
1 5 10 15

ttt ggt gtc caa cac gaa ttt cag cat gtc ctt ttc att gta ctt ctt 96
Phe Gly Val Gln His Glu Phe Gln His Val Leu Phe Ile Val Leu Leu
20 25 30

ctt atc tat gtg acc tcc ctg ata gga aat att gga atg atc tta ctc 144
Leu Ile Tyr Val Thr Ser Leu Ile Gly Asn Ile Gly Met Ile Leu Leu
35 40 45

atc aag acc gat tcc aga ctt caa aca ccc atg tac ttt ttt cca caa 192
Ile Lys Thr Asp Ser Arg Leu Gln Thr Pro Met Tyr Phe Phe Pro Gln
50 55 60

cat ttg gct ttt gtt gat atc tgt tat act tct gct atc act ccc aag 240
His Leu Ala Phe Val Asp Ile Cys Tyr Thr Ser Ala Ile Thr Pro Lys
65 70 75 80

atg ctc caa agc ttc aca gaa aat aat ttg ata aca ttt cgg ggc 288
Met Leu Gln Ser Phe Thr Glu Asn Asn Leu Ile Thr Phe Arg Gly
85 90 95

tgt gtg ata caa ttc tta gtt tat gca aca ttt gca acc agt gac tgt 336
Cys Val Ile Gln Phe Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp Cys
100 105 110

tac ctc cta gct att atg gca atg gat tgt tat gtt gcc atc tgt aag 384
Tyr Leu Leu Ala Ile Met Ala Met Asp Cys Tyr Val Ala Ile Cys Lys
115 120 125

ccc ctt cgc tat ccc atg atc atg tcc caa aca gtc tac atc caa ctc 432
Pro Leu Arg Tyr Pro Met Ile Met Ser Gln Thr Val Tyr Ile Gln Leu
130 135 140

gta gct ggc tca tat att ata ggc tca ata aat gcc tct gta cat aca 480
Val Ala Gly Ser Tyr Ile Ile Gly Ser Ile Asn Ala Ser Val His Thr
145 150 155 160

ggt ttt aca ttt tca ctg tcc ttc tgc aag tct aat aaa atc aat cac 528
Gly Phe Thr Phe Ser Leu Ser Phe Cys Lys Ser Asn Lys Ile Asn His
165 170 175

ttt ttc tgt gat ggt ctc cca att ctt gcc ctt tca tgc tcc aac att 576
Phe Phe Cys Asp Gly Leu Pro Ile Leu Ala Leu Ser Cys Ser Asn Ile
180 185 190

gac atc aac atc att cta gat gtt gtc ttt gtg gga ttt gac ttg atg 624
Asp Ile Asn Ile Leu Asp Val Val Phe Val Gly Phe Asp Leu Met
195 200 205

ttc act gag ttg gtc atc atc ttt tcc tac atc tac att atg gtc acc 672
Phe Thr Glu Leu Val Ile Ile Phe Ser Tyr Ile Tyr Ile Met Val Thr
210 215 220

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atc ctg aag atg tct tct act gct ggg agg aaa aaa tcc ttc tcc aca 720
 Ile Leu Lys Met Ser Ser Thr Ala Gly Arg Lys Ser Phe Ser Thr
 225 230 235 240

tgt gcc tcc cac ctg aca gca gta acc att ttc tat ggg aca ctc tct 768
 Cys Ala Ser His Leu Thr Ala Val Thr Ile Phe Tyr Gly Thr Leu Ser
 245 250 255

tac atg tac tta cag cct cag tct aat aat tct cag gag aat atg aaa 816
 Tyr Met Tyr Leu Gln Pro Gln Ser Asn Asn Ser Gln Glu Asn Met Lys
 260 265 270

gta gcc tct ata ttt tat ggc act gtt att ccc atg ttg aat cct tta 864
 Val Ala Ser Ile Phe Tyr Gly Thr Val Ile Pro Met Leu Asn Pro Leu
 275 280 285

atc tat agc ttg aga aat aag gaa gga aaa taa 897
 Ile Tyr Ser Leu Arg Asn Lys Glu Gly Lys
 290 295

<210> 186

<211> 298

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<400> 186

Met Gly Arg Gly Asn Ser Thr Glu Val Thr Glu Phe His Leu Leu Gly
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Leu Ile Tyr Val Thr Ser Leu Ile Gly Asn Ile Gly Met Ile Leu Leu
 35 40 45

Ile Lys Thr Asp Ser Arg Leu Gln Thr Pro Met Tyr Phe Phe Pro Gln
 50 55 60

His Leu Ala Phe Val Asp Ile Cys Tyr Thr Ser Ala Ile Thr Pro Lys
 65 70 75 80

Met Leu Gln Ser Phe Thr Glu Glu Asn Asn Leu Ile Thr Phe Arg Gly
 85 90 95

Cys Val Ile Gln Phe Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp Cys
 100 105 110

Tyr Leu Leu Ala Ile Met Ala Met Asp Cys Tyr Val Ala Ile Cys Lys
 115 120 125

Pro Leu Arg Tyr Pro Met Ile Met Ser Gln Thr Val Tyr Ile Gln Leu.
 130 135 140

Val Ala Gly Ser Tyr Ile Ile Gly Ser Ile Asn Ala Ser Val His Thr
 145 150 155 160

Gly Phe Thr Phe Ser Leu Ser Phe Cys Lys Ser Asn Lys Ile Asn His
 165 170 175

Phe Phe Cys Asp Gly Leu Pro Ile Leu Ala Leu Ser Cys Ser Asn Ile
 180 185 190

Asp Ile Asn Ile Ile Leu Asp Val Val Phe Val Gly Phe Asp Leu Met
 195 200 205

16U 200 PCT FINAL.ST25

Phe Thr Glu Leu Val Ile Ile Phe Ser Tyr Ile Tyr Ile Met Val Thr
 210 215 220

Ile Leu Lys Met Ser Ser Thr Ala Gly Arg Lys Lys Ser Phe Ser Thr
 225 230 235 240

Cys Ala Ser His Leu Thr Ala Val Thr Ile Phe Tyr Gly Thr Leu Ser
 245 250 255

Tyr Met Tyr Leu Gln Pro Gln Ser Asn Asn Ser Gln Glu Asn Met Lys
 260 265 270

Val Ala Ser Ile Phe Tyr Gly Thr Val Ile Pro Met Leu Asn Pro Leu
 275 280 285

Ile Tyr Ser Leu Arg Asn Lys Glu Gly Lys
 290 295

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ttt ggt gcc cag cat gag ttt tgg tgt atc ctc ttc att gta ttc ctt 96
 Phe Gly Ala Gln His Glu Phe Trp Cys Ile Leu Phe Ile Val Phe Leu
 20 25 30

ctc atc tat gtg acc tcc ata atg ggt aat agt gga ata atc tta ctc 144
 Leu Ile Tyr Val Thr Ser Ile Met Gly Asn Ser Gly Ile Ile Leu Leu
 35 40 45

atc aac aca gat tcc aga ttt caa aca ctc acg tac ttt ttt cta cca 192
 Ile Asn Thr Asp Ser Arg Phe Gln Thr Leu Thr Tyr Phe Phe Leu Gln
 50 55 60

cat ttg gct ttt gtt gat atc tgt tac act tct gct atc act ccc aag 240
 His Leu Ala Phe Val Asp Ile Cys Tyr Thr Ser Ala Ile Thr Pro Lys
 65 70 75 80

atg ctc caa agc ttc aca gaa gaa aag aat ttg atg tta ttt cag ggc 288
 Met Leu Gln Ser Phe Thr Glu Glu Lys Asn Leu Met Leu Phe Gln Gly
 85 90 95

tgt gtg ata caa ttc tta gtt tat gca aca ttt gca acc agt gac tgt 336
 Cys Val Ile Gln Phe Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp Cys
 100 105 110

tat ctc ctg gct atg atg gca gtg gat cct tat gtt gcc atc tgt aag 384
 Tyr Leu Ala Met Met Ala Val Asp Pro Tyr Val Ala Ile Cys Lys
 115 120 125

ccc ctt cac tat act gta atc atg tcc cga aca gtc tgc atc cgt ttg 432
 Pro Leu His Tyr Thr Val Ile Met Ser Arg Thr Val Cys Ile Arg Leu
 130 135 140

gta gct ggt tca tac atc atg ggc tca ata aat gcc tct gta caa aca 480
 Val Ala Gly Ser Tyr Ile Met Gly Ser Ile Asn Ala Ser Val Gln Thr
 145 150 155 160

ggt ttt aca tgt tca ctg tcc ttc tgc aag tcc aat agc atc aat cac 528
 Gly Phe Thr Cys Ser Leu Ser Phe Cys Lys Ser Asn Ser Ile Asn His

160 200 PCT FINAL.ST25
 165 170 175

ttt ttc tgt gat gtt ccc cct att ctt gct ctt tca tgc tcc aat gtt 576
 Phe Phe Cys Asp Val Pro Pro Ile Leu Ala Leu Ser Cys Ser Asn Val
 180 185 190

gac atc aac atc atg cta ctt gtt gtc ttt gtg gga tct aac ttg ata 624
 Asp Ile Asn Ile Met Leu Leu Val Val Phe Val Gly Ser Asn Leu Ile
 195 200 205

ttc act ggg ttg gtc gtc atc ttt tcc tac atc tac atc atg gcc acc 672
 Phe Thr Gly Leu Val Val Ile Phe Ser Tyr Ile Tyr Ile Met Ala Thr
 210 215 220

atc ctg aaa atg tct tct agt gca gga agg aaa aaa tcc ttc tca aca 720
 Ile Leu Lys Met Ser Ser Ser Ala Gly Arg Lys Lys Ser Phe Ser Thr
 225 230 235 240

tgt gct tcc cac ctg acc gca gtc acc att ttc tat ggg aca ccc tct 768
 Cys Ala Ser His Leu Thr Ala Val Thr Ile Phe Tyr Gly Thr Leu Ser
 245 250 255

tac atg tat ttg cag tct cat tct aat aat tcc cag gaa aat atg aaa 816
 Tyr Met Tyr Leu Gln Ser His Ser Asn Asn Ser Gln Glu Asn Met Lys
 260 265 270

gtg gcc ttt ata ttt tat ggc aca gtt att ccc atg tta aat cct tta 864
 Val Ala Phe Ile Phe Tyr Gly Thr Val Ile Pro Met Leu Asn Pro Leu
 275 280 285

atc tat agc ttg aga aat aag gaa gta aaa gaa gct tta aaa gtg ata 912
 Ile Tyr Ser Leu Arg Asn Lys Glu Val Lys Glu Ala Leu Lys Val Ile
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ggg aaa aag tta ttt taa 930
 Gly Lys Lys Leu Phe
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Leu Ile Tyr Val Thr Ser Ile Met Gly Asn Ser Gly Ile Ile Leu Leu
 35 40 45

Ile Asn Thr Asp Ser Arg Phe Gln Thr Leu Thr Tyr Phe Phe Leu Gln
 50 55 60

His Leu Ala Phe Val Asp Ile Cys Tyr Thr Ser Ala Ile Thr Pro Lys
 65 70 75 80

Met Leu Gln Ser Phe Thr Glu Glu Lys Asn Leu Met Leu Phe Gln Gly
 85 90 95

Cys Val Ile Gln Phe Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp,Cys
 100 105 110

Tyr Leu Leu Ala Met Met Ala Val Asp Pro Tyr Val Ala Ile Cys Lys
 115 120 125

Pro Leu His Tyr Thr Val Ile Met Ser Arg Thr Val Cys Ile Arg Leu

160 200 PCT FINAL.ST25
 130 135 140

Val Ala Gly Ser Tyr Ile Met Gly Ser Ile Asn Ala Ser Val Gln Thr
 145 150 155 160

Gly Phe Thr Cys Ser Leu Ser Phe Cys Lys Ser Asn Ser Ile Asn His
 165 170 175

Phe Phe Cys Asp Val Pro Pro Ile Leu Ala Leu Ser Cys Ser Asn Val
 180 185 190

Asp Ile Asn Ile Met Leu Leu Val Val Phe Val Gly Ser Asn Leu Ile
 195 200 205

Phe Thr Gly Leu Val Val Ile Phe Ser Tyr Ile Tyr Ile Met Ala Thr
 210 215 220

Ile Leu Lys Met Ser Ser Ser Ala Gly Arg Lys Lys Ser Phe Ser Thr
 225 230 235 240

Cys Ala Ser His Leu Thr Ala Val Thr Ile Phe Tyr Gly Thr Leu Ser
 245 250 255

Tyr Met Tyr Leu Gln Ser His Ser Asn Asn Ser Gln Glu Asn Met Lys
 260 265 270

Val Ala Phe Ile Phe Tyr Gly Thr Val Ile Pro Met Leu Asn Pro Leu
 275 280 285

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Gly Lys Lys Leu Phe
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 1 5 10 15

tgc atg ata caa tta ttg gtt tat gca aca ttt gca acc agt gac tgt 96
Cys Met Ile Gln Leu Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp Cys
 20 25 30

tat ctc ctg gct atg ata gca gtg gac cat tat gtt gca afc tgt aag 144
Tyr Leu Leu Ala Met Ile Ala Val Asp His Tyr Val Ala Ile Cys Lys
 35 40 45

ccc ctt cac tat acc gta atc acg tcc caa aca gtc tgc atc cat ttg 192
Pro Leu His Tyr Thr Val Ile Thr Ser Gln Thr Val Cys Ile His Leu
 50 55 60

gta gct ggt tca tac atc atg ggc tca ata aat gcc tct gta cat aca 240
Val Ala Gly Ser Tyr Ile Met Gly Ser Ile Asn Ala Ser Val His Thr
 65 70 75 80

ggt ttt gca ttt tca ctg tct ttc tgc aag tcc aat aac atc aac cac 288

160 200 PCT FINAL.ST2S

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|---|-----|-----|
| Gly Phe Ala Phe Ser Leu Ser Phe Cys Lys Ser Asn Asn Ile Asn His | | |
| 85 | 90 | 95 |
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| Phe Phe Cys Asp Gly Pro Pro Ile Leu Ala Leu Ser Cys Ser Asn Ile | | |
| 100 | 105 | 110 |
| gac atc aac atc atg cta ctt gtt gtc ttt gtg gga ttt aac ttg atg | | |
| Asp Ile Asn Ile Met Leu Leu Val Val Phe Val Gly Phe Asn Leu Met | | |
| 115 | 120 | 125 |
| ttc act ggg ttg gag aat atg aaa gtg gcc tct ata ttt tat ggc act | | |
| Phe Thr Gly Leu Glu Asn Met Lys Val Ala Ser Ile Phe Tyr Gly Thr | | |
| 130 | 135 | 140 |
| gtt att ccc atg ttg aat cct tta atc tat agc ttg aga aat aag gaa | | |
| Val Ile Pro Met Leu Asn Pro Leu Ile Tyr Ser Leu Arg Asn Lys Glu | | |
| 145 | 150 | 155 |
| gta aaa gaa gct tta aaa ttg ata ggg aaa aag ttc ttt taa | | |
| Val Lys Glu Ala Leu Lys Leu Ile Gly Lys Lys Phe Phe | | |
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<211> 173
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Cys Met Ile Gln Leu Leu Val Tyr Ala Thr Phe Ala Thr Ser Asp Cys
20 25 30

Tyr Leu Leu Ala Met Ile Ala Val Asp His Tyr Val Ala Ile Cys Lys
35 40 45

Pro Leu His Tyr Thr Val Ile Thr Ser Gln Thr Val Cys Ile His Leu
50 55 60

Val Ala Gly Ser Tyr Ile Met Gly Ser Ile Asn Ala Ser Val His Thr
65 70 75 80

Gly Phe Ala Phe Ser Leu Ser Phe Cys Lys Ser Asn Asn Ile Asn His
85 90 95

Phe Phe Cys Asp Gly Pro Pro Ile Leu Ala Leu Ser Cys Ser Asn Ile
100 105 110

Asp Ile Asn Ile Met Leu Leu Val Val Phe Val Gly Phe Asn Leu Met
115 120 125

Phe Thr Gly Leu Glu Asn Met Lys Val Ala Ser Ile Phe Tyr Gly Thr
130 135 140

Val Ile Pro Met Leu Asn Pro Leu Ile Tyr Ser Leu Arg Asn Lys Glu
145 150 155 160

Val Lys Glu Ala Leu Lys Leu Ile Gly Lys Lys Phe Phe
165 170

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16U 200 PCT FINAL.ST25

16U 200 PCT FINAL.ST25

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cgg gcc aca ttc cca gag tta tgt gcc agt ctt gtt gag gct tca cac 96
Arg Ala Thr Phe Pro Glu Leu Cys Ala Ser Leu Val Glu Ala Ser His
20 25 30

ctt ggc ggc ttt gta aac tca acc atc atc acc agt gag aca cct acc 144
Leu Gly Gly Phe Val Asn Ser Thr Ile Ile Thr Ser Glu Thr Pro Thr
35 40 45

tgt agc ttc tgt ggc agc aat atc att gat gat ttc ttc tgt gat ctg 192
Leu Ser Phe Cys Gly Ser Asn Ile Ile Asp Asp Phe Phe Cys Asp Leu
50 55 60

ccc cca ctt gta aag ttg gtg tgt gat gtg aag gag cgc tac cag gct 240
Pro Pro Leu Val Lys Leu Val Cys Asp Val Lys Glu Arg Tyr Gln Ala
65 70 75 80

gtg ctg cat ttt atg ctt gcc tcc aat cat cac tcc cac tgc act tat 288
Val Leu His Phe Met Leu Ala Ser Asn His His Ser His Cys Thr Tyr
85 90 95

tct tgc gtc cat ctc ttc atc att gca gcc atc tcg aag atc cgt tcc 336
Ser Cys Val His Leu Phe Ile Ile Ala Ala Ile Ser Lys Ile Arg Ser
100 105 110

att aag ggc cgc ctc cag gtc ttc tcc act tgt ggg tct ccc ctg acg 384
Ile Lys Gly Arg Leu Gln Val Phe Ser Thr Cys Gly Ser Pro Leu Thr
115 120 125

gct ctc acc ttg tac tat ggt gca atc ttc ttt att tac tcc caa cca 432
Ala Leu Thr Leu Tyr Tyr Gly Ala Ile Phe Phe Ile Tyr Ser Gln Pro
130 135 140

aga act agc tat gcc tta aaa atg gat aaa ttg ggg tca gtg ttc tat 480
Arg Thr Ser Tyr Ala Leu Lys Met Asp Lys Leu Gly Ser Val Phe Tyr
145 150 155 160

act gtg gtg att cca atg cta aac ccc ttg atc tat agc tta aga aat 528
Thr Val Val Ile Pro Met Leu Asn Pro Leu Ile Tyr Ser Leu Arg Asn
165 170 175

aag gat gtc aaa gat gcc ttg aag aaa atg tta gat aga ctt cag ttt 576
Lys Asp Val Lys Asp Ala Leu Lys Lys Met Leu Asp Arg Leu Gln Phe
180 185 190

ctt aaa gaa aaa tat tgt aga tat ggg ctg gcc tgt agt gag cgc tac 624
Leu Lys Glu Lys Tyr Cys Arg Tyr Gly Leu Ala Cys Ser Glu Arg Tyr
195 200 205

ctc ctg gct gcc atg ggt tat gac tgc tat gag gca atc tcc aag ccc 672
Leu Leu Ala Ala Met Gly Tyr Asp Cys Tyr Glu Ala Ile Ser Lys Pro
210 215 220

ctg ctt taa 681
Leu Leu
225

<210> 194
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<400> 194

16U 200 PCT FINAL.ST25

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| Arg Ala Thr Phe Pro Glu Leu Cys Ala Ser Leu Val Glu Ala Ser His | |
| 20 | 25 |
| Leu Gly Gly Phe Val Asn Ser Thr Ile Ile Thr Ser Glu Thr Pro Thr | |
| 35 | 40 |
| Leu Ser Phe Cys Gly Ser Asn Ile Ile Asp Asp Phe Phe Cys Asp Leu | |
| 50 | 55 |
| Pro Pro Leu Val Lys Leu Val Cys Asp Val Lys Glu Arg Tyr Gln Ala | |
| 65 | 70 |
| Val Leu His Phe Met Leu Ala Ser Asn His His Ser His Cys Thr Tyr | |
| 85 | 90 |
| Ser Cys Val His Leu Phe Ile Ile Ala Ala Ile Ser Lys Ile Arg Ser | |
| 100 | 105 |
| Ile Lys Gly Arg Leu Gln Val Phe Ser Thr Cys Gly Ser Pro Leu Thr | |
| 115 | 120 |
| Ala Leu Thr Leu Tyr Tyr Gly Ala Ile Phe Phe Ile Tyr Ser Gln Pro | |
| 130 | 135 |
| Arg Thr Ser Tyr Ala Leu Lys Met Asp Lys Leu Gly Ser Val Phe Tyr | |
| 145 | 150 |
| Thr Val Val Ile Pro Met Leu Asn Pro Leu Ile Tyr Ser Leu Arg Asn | |
| 165 | 170 |
| Lys Asp Val Lys Asp Ala Leu Lys Lys Met Leu Asp Arg Leu Gln Phe | |
| 180 | 185 |
| Leu Lys Glu Lys Tyr Cys Arg Tyr Gly Leu Ala Cys Ser Glu Arg Tyr | |
| 195 | 200 |
| Leu Leu Ala Ala Met Gly Tyr Asp Cys Tyr Glu Ala Ile Ser Lys Pro | |
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| Leu Leu | |
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| 1 | 5 |
| 10 | 15 |
| tcg gat gcc ggc acc agc tgc ccc gtc ctt tgc aca tgc cgt aac cag | 96 |
| Ser Asp Ala Gly Thr Ser Cys Pro Val Leu Cys Thr Cys Arg Asn Gln | |
| 20 | 25 |
| 25 | 30 |

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| | |
|---|------|
| gtg gtg gat tgt agc agc cag cgg cta ttc tcc gtg ccc cca gac ctg Val Val Asp Cys Ser Ser Gln Arg Leu Phe Ser Val Pro Pro Asp Leu 35 40 45 | 144 |
| cca atg gac acc cga aac ctc agc ctg gcc cac aac cgc atc aca gca Pro Met Asp Thr Arg Asn Leu Ser Leu Ala His Asn Arg Ile Thr Ala 50 55 60 | 192 |
| gtg ccg cct ggc tac ctc aca tgc tac atg gag ctc cag gtg ctg gat Val Pro Pro Gly Tyr Leu Thr Cys Tyr Met Glu Leu Gln Val Leu Asp 65 70 75 80 | 240 |
| ttg cac aac aac tcc tta atg gag ctg ccc cgg ggc ctc ttc ctc cat Leu His Asn Asn Ser Leu Met Glu Leu Pro Arg Gly Leu Phe Leu His 85 90 95 | 288 |
| gcc aag cgc ttg gca cac ttg gac ctg agc tac aac aat ttc agc cat Ala Lys Arg Leu Ala His Leu Asp Leu Ser Tyr Asn Asn Phe Ser His 100 105 110 | 336 |
| gtg cca gcc gac atg ttc cag gag gcc cat ggg cta gtc cac atc gac Val Pro Ala Asp Met Phe Gln Glu Ala His Gly Leu Val His Ile Asp 115 120 125 | 384 |
| ctg agc cac aac ccc tgg ctg cgg agg gtg cat ccc cag gcc ttt cag Leu Ser His Asn Pro Trp Leu Arg Arg Val His Pro Gln Ala Phe Gln 130 135 140 | 432 |
| ggc ctc atg cag ctc cga gac ctg gac ctc agt tat ggg ggc ctg gcc Gly Leu Met Gln Leu Arg Asp Leu Asp Leu Ser Tyr Gly Gly Leu Ala 145 150 155 160 | 480 |
| ttc ctc agc ctg gag gct ctt gag ggc cta ccg ggg ctg gtg acc ctg Phe Leu Ser Leu Glu Ala Leu Glu Gly Leu Pro Gly Leu Val Thr Leu 165 170 175 | 528 |
| cag atc ggt ggc aat ccc tgg gtg tgt ggc tgc acc atg gaa ccc ctg Gln Ile Gly Gly Asn Pro Trp Val Cys Gly Cys Thr Met Glu Pro Leu 180 185 190 | 576 |
| ctg aag tgg ctg cga aac cgg atc cag cgc tgt aca gca gag tca ggt Leu Lys Trp Leu Arg Asn Arg Ile Gln Arg Cys Thr Ala Glu Ser Gly 195 200 205 | 624 |
| tct ggc ctg ccc gaa gag tca gaa cct gag tcc tgg act ggc caa agg Ser Gly Leu Pro Glu Glu Ser Glu Pro Glu Ser Trp Thr Gly Gln Arg 210 215 220 | 672 |
| gct gca gta gag ttc cag gac ctc atg cag ctc caa gac ctg gat ctc Ala Ala Val Glu Phe Gln Asp Leu Met Gln Leu Gln Asp Leu Asp Leu 225 230 235 240 | 720 |
| agc tac gag aac ctg gct ttc ctc aaa ctc aag gcc ctg agc agt gta Ser Tyr Glu Asn Leu Ala Phe Leu Lys Leu Lys Ala Leu Ser Ser Val 245 250 255 | 768 |
| aac ttt ggg cac agg caa gcg gtt gtg ggt gga ctt tcc aat ccc ctc Asn Phe Gly His Arg Gln Ala Val Val Gly Gly Leu Ser Asn Pro Leu 260 265 270 | 816 |
| tcc ttc cct ggg tac ctc acc ctc cct ggc ttc tgt gtt aca gat tct Ser Phe Pro Gly Tyr Leu Thr Leu Pro Gly Phe Cys Val Thr Asp Ser 275 280 285 | 864 |
| cag ctg gct gag tgc cgg ggc cct cct gaa gtc gag ggc gcc ccc ctc Gln Leu Ala Glu Cys Arg Gly Pro Pro Glu Val Glu Gly Ala Pro Leu 290 295 300 | 912 |
| ttc tca ctc act gag gag agc ttc aag gcc tgc cac ctg acc ctg acc Phe Ser Leu Thr Glu Glu Ser Phe Lys Ala Cys His Leu Thr Leu Thr 305 310 315 320 | 960 |
| ctg gat gat tac cta ttc att gcg ttc gtg ggc ttc gtg gtc tcc att Leu Asp Asp Tyr Leu Phe Ile Ala Phe Val Gly Phe Val Val Ser Ile 325 330 335 | 1008 |
| gct tct gtg gcc acc aac ttc ctc ctg ggc atc act gcc aac tgc tgc Ala Ser Val Ala Thr Asn Phe Leu Leu Gly Ile Thr Ala Asn Cys Cys 340 345 350 | 1056 |

16U 200 PCT FINAL.ST25

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<400> 196

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Val Val Asp Cys Ser Ser Gln Arg Leu Phe Ser Val Pro Pro Asp Leu
 35 40 45

Pro Met Asp Thr Arg Asn Leu Ser Leu Ala His Asn Arg Ile Thr Ala
 50 55 60

Val Pro Pro Gly Tyr Leu Thr Cys Tyr Met Glu Leu Gln Val Leu Asp
 65 70 75 80

Leu His Asn Asn Ser Leu Met Glu Leu Pro Arg Gly Leu Phe Leu His
 85 90 95

Ala Lys Arg Leu Ala His Leu Asp Leu Ser Tyr Asn Asn Phe Ser His
 100 105 110

Val Pro Ala Asp Met Phe Gln Glu Ala His Gly Leu Val His Ile Asp
 115 120 125

Leu Ser His Asn Pro Trp Leu Arg Arg Val His Pro Gln Ala Phe Gln
 130 135 140

Gly Leu Met Gln Leu Arg Asp Leu Asp Leu Ser Tyr Gly Leu Ala
 145 150 155 160

Phe Leu Ser Leu Glu Ala Leu Glu Gly Leu Pro Gly Leu Val Thr Leu
 165 170 175

Gln Ile Gly Gly Asn Pro Trp Val Cys Gly Cys Thr Met Glu Pro Leu
 180 185 190

Leu Lys Trp Leu Arg Asn Arg Ile Gln Arg Cys Thr Ala Glu Ser Gly
 195 200 205

Ser Gly Leu Pro Glu Glu Ser Glu Pro Glu Ser Trp Thr Gly Gln Arg
 210 215 220

Ala Ala Val Glu Phe Gln Asp Leu Met Gln Leu Gln Asp Leu Asp Leu
 225 230 235 240

Ser Tyr Glu Asn Leu Ala Phe Leu Lys Leu Lys Ala Leu Ser Ser Val
 245 250 255

Asn Phe Gly His Arg Gln Ala Val Val Gly Gly Leu Ser Asn Pro Leu
 260 265 270

160 200 PCT FINAL ST25

Ser Phe Pro Gly Tyr Leu Thr Leu Pro Gly Phe Cys Val Thr Asp Ser
275 280 285

Gln Leu Ala Glu Cys Arg Gly Pro Pro Glu Val Glu Gly Ala Pro Leu
290 295 300

Phe Ser Leu Thr Glu Glu Ser Phe Lys Ala Cys His Leu Thr Leu Thr
305 310 315 320

Leu Asp Asp Tyr Leu Phe Ile Ala Phe Val Gly Phe Val Val Ser Ile
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34

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35

<210> 202
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33

16U 200 PCT FINAL.ST25

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| <210> 213 | |
| <211> 50 | |
| <212> DNA | |
| <213> Homo sapiens | |
| <400> 213 | |
| cacacacaca tatatatatac cacacatata tttataatca tttaacaaca | 50 |
| <210> 214 | |
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| <400> 214 | |
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| 5 10 15 | |
| ttc act gaa tat cct gaa tgg gca ctc cct ctc ttc ttg ttt tta Phe Thr Glu Tyr Pro Glu Trp Ala Leu Pro Leu Phe Leu Leu Phe Leu | 96 |
| 20 25 30 | |
| ttt atg tat ctc atc acc gta ttg ggg aac tta gag atg att att ctg Phe Met Tyr Leu Ile Thr Val Leu Gly Asn Leu Glu Met Ile Ile Leu | 144 |
| 35 40 45 | |
| atc ctc atg gat cac cag ctc cac gct cca atg tat ttc ctt ctg agt Ile Leu Met Asp His Gln Leu His Ala Pro Met Tyr Phe Leu Leu Ser | 192 |
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| 165 170 175 | |
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Cys Ala Ala Gln Phe Phe Leu Phe Thr Phe Phe Gly Ser Ile Asp Cys
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Tyr Leu Leu Ala Leu Met Ala Tyr Asp Arg Tyr Leu Ala Val Cys Gln
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Phe Tyr Thr Leu Thr Leu Leu Gly Asn Gly Val Ile Phe Gly Ile Ile
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Thr Tyr Met Ala Pro Lys Ser Arg His Pro Glu Glu Gln Gln Lys Val
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| Asn Leu Ser Phe Leu Asp Leu Cys Tyr Gly Thr Ala Ser Met Pro Gln | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Ala Leu Val His Cys Phe Ser Thr His Pro Tyr Leu Ser Tyr Pro Arg | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Leu Leu Ala Ala Met Ala Tyr Asp Arg Val Val Ala Ile Ser Asn | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 115 | 120 | 125 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ccc ctg cgt tat tca gtg gtt atg aat ggc cca gta tgt gtc tgc ttg | 432 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Pro Leu Arg Tyr Ser Val Val Met Asn Gly Pro Val Cys Val Cys Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 130 | 135 | 140 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Val Ala Thr Ser Trp Gly Thr Ser Leu Val Leu Thr Ala Met Leu Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 145 | 150 | 155 | 160 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| cta tcc ctg agg ctt cac ttc tgt ggg gct aat gtc atc aac cat ttt | 528 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Ser Leu Arg Leu His Phe Cys Gly Ala Asn Val Ile Asn His Phe | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 165 | 170 | 175 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| gcc tgt gag att ctc tcc ctc att aag ctg acc tgt tct gat acc agc | 576 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Ala Cys Glu Ile Leu Ser Leu Ile Lys Leu Thr Cys Ser Asp Thr Ser | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 180 | 185 | 190 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ctc aat gaa ttt atg atc ctc atc acc agt atc ttc acc ctg ctg cta | 624 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Asn Glu Phe Met Ile Leu Ile Thr Ser Ile Phe Thr Leu Leu Leu | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 195 | 200 | 205 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Pro Phe Gly Phe Val Leu Leu Ser Tyr Ile Arg Ile Ala Met Ala Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 210 | 215 | 220 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Ile Arg Ile Arg Ser Leu Gln Gly Arg Leu Lys Ala Phe Thr Thr Cys | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 225 | 230 | 235 | 240 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ggc tct cac ctg acc gtg gtg aca atc ttc tat ggg tca gcc atc tcc | 768 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Gly Ser His Leu Leu Val Val Thr Ile Phe Tyr Gly Ser Ala Ile Ser | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 245 | 250 | 255 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| atg tat atg aaa act cag tcc aag tcc tac cct gac cag gac aag ttt | 816 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| -Met Tyr Met Lys Thr Gln Ser Lys Ser Tyr Pro Asp Gln Asp Lys Phe | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 260 | 265 | 270 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| Ile Ser Val Phe Tyr Gly Ala Leu Thr Pro Met Leu Asn Pro Leu Ile | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 275 | 280 | 285 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| tat agc ctg aga aaa aaa gat gtt aaa cgg gca ata agg aaa gtt atg | 912 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Tyr Ser Leu Arg Lys Lys Asp Val Lys Arg Ala Ile Arg Lys Val Met | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 290 | 295 | 300 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| ttg aaa agg aca tga | 927 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Leu Lys Arg Thr | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 305 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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Ile Ile Tyr Leu Ser Thr Leu Leu Gly Asn Gly Phe Met Ile Phe Leu
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Ile His Phe Asp Pro Asn Leu His Thr Pro Ile Tyr Phe Phe Leu Ser
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Asn Leu Ser Phe Leu Asp Leu Cys Tyr Gly Thr Ala Ser Met Pro Gln
 65 70 75 80

Ala Leu Val His Cys Phe Ser Thr His Pro Tyr Leu Ser Tyr Pro Arg
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Cys Leu Ala Gln Thr Ser Val Ser Leu Ala Leu Ala Thr Ala Glu Cys
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Leu Leu Leu Ala Ala Met Ala Tyr Asp Arg Val Val Ala Ile Ser Asn
 115 120 125

Pro Leu Arg Tyr Ser Val Val Met Asn Gly Pro Val Cys Val Cys Leu
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Val Ala Thr Ser Trp Gly Thr Ser Leu Val Leu Thr Ala Met Leu Ile
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Leu Ser Leu Arg Leu His Phe Cys Gly Ala Asn Val Ile Asn His Phe
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Ala Cys Glu Ile Leu Ser Leu Ile Lys Leu Thr Cys Ser Asp Thr Ser
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Leu Asn Glu Phe Met Ile Leu Ile Thr Ser Ile Phe Thr Leu Leu Leu
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Pro Phe Gly Phe Val Leu Leu Ser Tyr Ile Arg Ile Ala Met Ala Ile
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Ile Arg Ile Arg Ser Leu Gln Gly Arg Leu Lys Ala Phe Thr Thr Cys
 225 230 235 240

Gly Ser His Leu Thr Val Val Thr Ile Phe Tyr Gly Ser Ala Ile Ser
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Met Tyr Met Lys Thr Gln Ser Lys Ser Tyr Pro Asp Gln Asp Lys Phe
 260 265 270

Ile Ser Val Phe Tyr Gly Ala Leu Thr Pro Met Leu Asn Pro Leu Ile
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Leu Lys Arg Thr
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| atc cac aag aat gat ggt gtc agt ctc tgc ttc acc ttg aat ctg gct Ile His Lys Asn Asp Gly Val Ser Leu Cys Phe Thr Leu Asn Leu Ala 35 40 45 | 144 |
| gtg gct gac acc ttg att ggt gtg gcc atc tct ggc cta ctc aca gac Val Ala Asp Thr Leu Ile Gly Val Ala Ile Ser Gly Leu Leu Thr Asp 50 55 60 | 192 |
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| tac ttg aag atc atg agt ggg ttc gtg gcc ggg gcc tgc att gcc ggg Tyr Leu Lys Ile Met Ser Gly Phe Val Ala Gly Ala Cys Ile Ala Gly 115 120 125 | 384 |
| ctg tgg tta gtg tct tac ctc att ggc ttc ctc cca ctc gga atc ccc Leu Trp Leu Val Ser Tyr Leu Ile Gly Phe Leu Pro Leu Gly Ile Pro 130 135 140 | 432 |
| atg ttc cag cag act gcc tac aaa ggg cag tgc agc ttc ttt gct gta Met Phe Gln Gln Thr Ala Tyr Lys Gly Gln Cys Ser Phe Phe Ala Val 145 150 155 160 | 480 |
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| - gcc atg ctc ctc ttt gtc ttc tac tgc gac atg ctc aag att gcc Ala Met Leu Leu Phe Val Phe Phe Tyr Cys Asp Met Leu Lys Ile Ala 180 185 190 | 576 |
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| cgt act gtg tct gtt ctc att ggg agc ttt gct cta tcc tgg acc ccc Arg Thr Val Ser Val Leu Ile Gly Ser Phe Ala Leu Ser Trp Thr Pro 225 230 235 240 | 720 |
| tcc ctt atc act ggc att gtg cag gtg gcc tgc cag gag tgt cac ctc Phe Leu Ile Thr Gly Ile Val Gln Val Ala Cys Gln Glu Cys His Leu 245 250 255 | 768 |

16U 200 PCT FINAL.ST25

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 260 265 270

ctg ctc aac cca ctc atc tat gcc tat tgg cag aag gag gtg cga ctg
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Ile His Lys Asn Asp Gly Val Ser Leu Cys Phe Thr Leu Asn Leu Ala
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Val Ala Asp Thr Leu Ile Gly Val Ala Ile Ser Gly Leu Leu Thr Asp
 50 55 60

Gln Leu Ser Ser Pro Ser Arg Pro Thr Gln Lys Thr Leu Cys Ser Leu
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Arg Met Ala Phe Val Thr Ser Ser Ala Ala Ser Val Leu Thr Val
 85 90 95

Met Leu Ile Thr Phe Asp Arg Tyr Leu Ala Ile Lys Gln Pro Phe Arg
 100 105 110

Tyr Leu Lys Ile Met Ser Gly Phe Val Ala Gly Ala Cys Ile Ala Gly
 115 120 125

Leu Trp Leu Val Ser Tyr Leu Ile Gly Phe Leu Pro Leu Gly Ile Pro
 130 135 140

Met Phe Gln Gln Thr Ala Tyr Lys Gly Gln Cys Ser Phe Phe Ala Val
 145 150 155 160

Phe His Pro His Phe Val Leu Thr Leu Ser Cys Val Gly Phe Phe Pro
 165 170 175

Ala Met Leu Leu Phe Val Phe Phe Tyr Cys Asp Met Leu Lys Ile Ala
 180 185 190

Ser Met His Ser Gln Gln Ile Arg Lys Met Glu His Ala Gly Ala Met
 195 200 205

16U 200 PCT FINAL.ST25

Ala Gly Gly Tyr Arg Ser Pro Arg Thr Pro Ser Asp Phe Lys Ala Leu
 210 215 220

Arg Thr Val Ser Val Leu Ile Gly Ser Phe Ala Leu Ser Trp Thr Pro
 225 230 235 240

Phe Leu Ile Thr Gly Ile Val Gln Val Ala Cys Gln Glu Cys His Leu
 245 250 255

Tyr Leu Val Leu Glu Arg Tyr Leu Trp Leu Leu Gly Val Gly Asn Ser
 260 265 270

Leu Leu Asn Pro Leu Ile Tyr Ala Tyr Trp Gln Lys Glu Val Arg Leu
 275 280 285

Gln Leu Tyr His Met Ala Leu Gly Val Lys Lys Val Leu Thr Ser Phe
 290 295 300

Leu Leu Phe Leu Ser Ala Arg Asn Cys Gly Pro Glu Arg Pro Arg Glu
 305 310 315 320

Ser Ser Cys His Ile Val Thr Ile Ser Ser Ser Glu Phe Asp Gly
 325 330 335

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<211> 975

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<213> Homo sapiens

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<222> (1)..(972)

<223>

<400> 222

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| atg cgg cct cag gac agc acc ggg gtc gcg gag ctc cag gag ccc ggg | 48 |
| Met Arg Pro Gln Asp Ser Thr Gly Val Ala Glu Leu Gln Glu Pro Gly | |
| 1 5 10 15 | |

| | |
|---|----|
| ctg ccg cta acg gac gat gca ccc ccg ggc gcc act gag gag ccg gcg | 96 |
| Leu Pro Leu Thr Asp Asp Ala Pro Pro Gly Ala Thr Glu Glu Pro Ala | |
| 20 25 30 | |

| | |
|---|-----|
| gcc gcc gag gca gct ggg gcg cca gac cgc gtg ggc tct tta ttt gtt | 144 |
| Ala Ala Glu Ala Ala Gly Ala Pro Asp Arg Val Gly Ser Leu Phe Val | |
| 35 40 45 | |

| | |
|---|-----|
| aaa aaa gtg caa gac gtc cat gct gta gag att agt gcg ttt cga tgt | 192 |
| Lys Lys Val Gln Asp Val His Ala Val Glu Ile Ser Ala Phe Arg Cys | |
| 50 55 60 | |

| | |
|---|-----|
| gtg ttc caa atg cta gtt gtt atc cct tgc tta ata tac aga aaa act | 240 |
| Val Phe Gln Met Leu Val Val Ile Pro Cys Leu Ile Tyr Arg Lys Thr | |
| 65 70 75 80 | |

| | |
|---|-----|
| ggg ttt ata ggc cca aaa ggt caa cga att ttc ctc att ctc aga gga | 288 |
| Gly Phe Ile Gly Pro Lys Gly Gln Arg Ile Phe Leu Ile Leu Arg Gly | |
| 85 90 95 | |

| | |
|---|-----|
| gtc ctt ggt tct acc gcc atg atg ctt ata tac tat gct tac cag aca | 336 |
| Val Leu Gly Ser Thr Ala Met Met Leu Ile Tyr Tyr Ala Tyr Gln Thr | |
| 100 105 110 | |

| | |
|---|-----|
| atg tcc ctc gct gat gcc aca gtt atc acg ttt agc agt cca gtg ttt | 384 |
| Met Ser Leu Ala Asp Ala Thr Val Ile Thr Phe Ser Ser Pro Val Phe | |
| 115 120 125 | |

| | |
|---|-----|
| acg tcc ata ttt gct tgg ata tgt ctc aag gaa aaa tat agc cct tgg | 432 |
| Thr Ser Ile Phe Ala Trp Ile Cys Leu Lys Glu Lys Tyr Ser Pro Trp | |

| 130 | 135 | 140 | 160 200 PCT FINAL.ST25 | |
|--|-----|-----|------------------------|-----|
| gat gct ctt ttc acc gtg ttc aca atc act gga gtg atc ctt atc gtg Asp Ala Leu Phe Thr Val Phe Thr Ile Thr Gly Val Ile Leu Ile Val | 145 | 150 | 155 | 480 |
| 145 | 150 | 155 | 160 | |
| aga cca cca ttt ttg ttt ggt tcc gac act tcg ggg atg gaa gaa agc Arg Pro Pro Phe Leu Phe Gly Ser Asp Thr Ser Gly Met Glu Glu Ser | 165 | 170 | 175 | 528 |
| 165 | 170 | 175 | | |
| tat tca ggc cac ctt aag gga aca ttc gca gca att gga agt gcc gta Tyr Ser Gly His Leu Lys Gly Thr Phe Ala Ala Ile Gly Ser Ala Val | 180 | 185 | 190 | 576 |
| 180 | 185 | 190 | | |
| ttt gct gca tcg act cta gtt atc cta aga aaa atg gga aaa tct gtg Phe Ala Ala Ser Thr Leu Val Ile Leu Arg Lys Met Gly Lys Ser Val | 195 | 200 | 205 | 624 |
| 195 | 200 | 205 | | |
| gac tac ttt ctg agc att tgg tat tat gta gta ctt ggc ctc gtt gaa Asp Tyr Phe Leu Ser Ile Trp Tyr Val Val Leu Gly Leu Val Glu | 210 | 215 | 220 | 672 |
| 210 | 215 | 220 | | |
| agt gtc atc atc ctc tct gta tta gga gag tgg agt ctg cct tac tgt Ser Val Ile Ile Leu Ser Val Leu Gly Glu Trp Ser Leu Pro Tyr Cys | 225 | 230 | 235 | 720 |
| 225 | 230 | 235 | 240 | |
| ggg ttg gac agg cta ttt ctc ata ttc att ggg ctc ttt ggt ttg ggg Gly Leu Asp Arg Leu Phe Leu Ile Phe Ile Gly Leu Phe Gly Leu Gly | 245 | 250 | 255 | 768 |
| 245 | 250 | 255 | | |
| ggt cag ata ttt atc aca aaa gca ctt caa ata gaa aaa gca ggg cca Gly Gln Ile Phe Ile Thr Lys Ala Leu Gln Ile Glu Lys Ala Gly Pro | 260 | 265 | 270 | 816 |
| 260 | 265 | 270 | | |
| gta gca ata atg aag aca atg gat gtc ttt gct ttt atc ttt cag Val Ala Ile Met Lys Thr Met Asp Val Val Phe Ala Phe Ile Phe Gln | 275 | 280 | 285 | 864 |
| 275 | 280 | 285 | | |
| att att ttc ttt aat aat gtg cca acg tgg tgg aca gtg ggt ggt gct Ile Ile Phe Phe Asn Asn Val Pro Thr Trp Trp Thr Val Gly Gly Ala | 290 | 295 | 300 | 912 |
| 290 | 295 | 300 | | |
| ctc tgc gta gta gcc agt aat gtt gga gcg gcc att cgt aaa tgg tac Leu Cys Val Val Ala Ser Asn Val Gly Ala Ala Ile Arg Lys Trp Tyr | 305 | 310 | 315 | 960 |
| 305 | 310 | 315 | 320 | |
| caa agt tcc aaa tga Gln Ser Ser Lys | | | | 975 |

<210> 223

<211> 324

<212> PRT

<213> Homo sapiens

<400> 223

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35 40 45Lys Lys Val Gln Asp Val His Ala Val Glu Ile Ser Ala Phe Arg Cys
50 55 60Val Phe Gln Met Leu Val Val Ile Pro Cys Leu Ile Tyr Arg Lys Thr
65 70 75 80

Gly Phe Ile Gly Pro Lys Gly Gln Arg Ile Phe Leu Ile Leu Arg Gly

85 90 16U 200 PCT FINAL ST25 95

Val Leu Gly Ser Thr Ala Met Met Leu Ile Tyr Tyr Ala Tyr Gln Thr
100 105 110

Met Ser Leu Ala Asp Ala Thr Val Ile Thr Phe Ser Ser Pro Val Phe
115 120 125

Thr Ser Ile Phe Ala Trp Ile Cys Leu Lys Glu Lys Tyr Ser Pro Trp
130 135 140

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asp | Ala | Leu | Phe | Thr | Val | Phe | Thr | Ile | Thr | Gly | Val | Ile | Leu | Ile | Val |
| 145 | | | | | 150 | | | | | 155 | | | | | 160 |

Arg Pro Pro Phe Leu Phe Gly Ser Asp Thr Ser Gly Met Glu Glu Ser
165 170 175

Tyr Ser Gly His Leu Lys Gly Thr Phe Ala Ala Ile Gly Ser Ala Val
180 185 190

Phe Ala Ala Ser Thr Leu Val Ile Leu Arg Lys Met Gly Lys Ser Val
195 200 205

Asp Tyr Phe Leu Ser Ile Trp Tyr Tyr Val Val Leu Gly Leu Val Glu
210 215 220

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Val | Ile | Ile | Leu | Ser | Val | Leu | Gly | Glu | Trp | Ser | Leu | Pro | Tyr | Cys |
| 225 | | | | 230 | | | | | | 235 | | | | | 240 |

Gly Leu Asp Arg Leu Phe Leu Ile Phe Ile Gly Leu Phe Gly Leu Gly
245 250 255

Gly Gln Ile Phe Ile Thr Lys Ala Leu Gln Ile Glu Lys Ala Gly Pro
260 265 270

Val Ala Ile Met Lys Thr Met Asp Val Val Phe Ala Phe Ile Phe Gln
275 280 285

Ile Ile Phe Phe Asn Asn Val Pro Thr Trp Trp Trp Thr Val Gly Gly Ala
290 295 300

Leu Cys Val Val Ala Ser Asn Val Gly Ala Ala Ile Arg Lys Trp Tyr
 305 310 315 320

Gln Ser Ser Lys

<210> 224
<211> 876
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Met Tyr Asn Met Ser Asp His Gly Thr Gly Leu Phe Ile Leu Leu Gly
1           5                   10                  15

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atc cct gga ctt gag cag tac cac gtc tgg atc agc atc cca ttc tgc 96

160_200 PCT FINAL.ST25

| | | | |
|---|-----|-----|-----|
| Ile Pro Gly Leu Glu Gln Tyr His Val Trp Ile Ser Ile Pro Phe Cys | | | |
| 20 | 25 | 30 | |
| tta atc tat ctc atg gct gtc gtg gcc aat agt atc ctt ctc tac ctc | | | |
| Leu Ile Tyr Leu Met Ala Val Val Ala Asn Ser Ile Leu Leu Tyr Leu | | | 144 |
| 35 | 40 | 45 | |
| att gtg gta gag cac agt ctt cat gca ccc atg ttc ttt ttc ctt tcc | | | |
| Ile Val Val Glu His Ser Leu His Ala Pro Met Phe Phe Phe Leu Ser | | | 192 |
| 50 | 55 | 60 | |
| atg ctg gcc att act gat ctc ata ttg tcc acc aca tgt gtc ccc aaa | | | |
| Met Leu Ala Ile Thr Asp Leu Ile Leu Ser Thr Thr Cys Val Pro Lys | | | 240 |
| 65 | 70 | 75 | 80 |
| aca ctt agc atc ttc tgc ttt gtg ttg gac tca gct ata ctg ctg gcc | | | |
| Thr Leu Ser Ile Phe Cys Phe Val Leu Asp Ser Ala Ile Leu Leu Ala | | | 288 |
| 85 | 90 | 95 | |
| atg gca ttt gac cgc tat atg gcc att tgc tca ccc ttg aga tac act | | | |
| Met Ala Phe Asp Arg Tyr Met Ala Ile Cys Ser Pro Leu Arg Tyr Thr | | | 336 |
| 100 | 105 | 110 | |
| act att ctg act ccc aaa acc att gtc aaa att gct gtg gga ata tgt | | | |
| Thr Ile Leu Thr Pro Lys Thr Ile Val Lys Ile Ala Val Gly Ile Cys | | | 384 |
| 115 | 120 | 125 | |
| ttc cga agt ttc tgt gtt ttt gtc cca tgt gtt ttc ctt gtg aat cgt | | | |
| Phe Arg Ser Phe Cys Val Phe Val Pro Cys Val Phe Leu Val Asn Arg | | | 432 |
| 130 | 135 | 140 | |
| tta ccc ttc tgc agg aca cat atc att tct cac aca tac tgt gag cac | | | |
| Leu Pro Phe Cys Arg Thr His Ile Ile Ser His Thr Tyr Cys Glu His | | | 480 |
| 145 | 150 | 155 | 160 |
| ata ggt gtt gcc cag ctt gcc tgt gct gat atc tcc atc aat atc tgg | | | |
| Ile Gly Val Ala Gln Leu Ala Cys Ala Asp Ile Ser Ile Asn Ile Trp | | | 528 |
| 165 | 170 | 175 | |
| tgt gga ttt tgt gtt ccc atc atg acg gtg atg aca gac gtg atc ctc | | | |
| Cys Gly Phe Cys Val Pro Ile Met Thr Val Met Thr Asp Val Ile Leu | | | 576 |
| 180 | 185 | 190 | |
| att gct gtc tcc tac acc ctc atc ctc tgt gct gtc ttt tgc ctc ccc | | | |
| Ile Ala Val Ser Tyr Thr Leu Ile Leu Cys Ala Val Phe Cys Leu Pro | | | 624 |
| 195 | 200 | 205 | |
| tcc caa gat gcc cgt cag aag gcc ctt tgc tcc tgt ggt tcc cat gtc | | | |
| Ser Gln Asp Ala Arg Gln Lys Ala Leu Cys Ser Cys Gly Ser His Val | | | 672 |
| 210 | 215 | 220 | |
| tgt gtt atc ctc ata ttc tat ata cca gca ttc ttc tcc att ctt gcc | | | |
| Cys Val Ile Leu Ile Phe Tyr Ile Pro Ala Phe Phe Ser Ile Leu Ala | | | 720 |
| 225 | 230 | 235 | 240 |
| cat tgc ttt ggg cat aat gtc cct cat acc ttt cat att atg ttt gcc | | | |
| His Cys Phe Gly His Asn Val Pro His Thr Phe His Ile Met Phe Ala | | | 768 |
| 245 | 250 | 255 | |
| aac ctt tat gta atc att cca cct gct ctc aac tct att gtc tac aga | | | |
| Asn Leu Tyr Val Ile Ile Pro Pro Ala Leu Asn Ser Ile Val Tyr Arg | | | 816 |
| 260 | 265 | 270 | |
| ata aag acc aag caa atc cag aac aga atc ctt ttg ctc ttt ccc aag | | | |
| Ile Lys Thr Lys Gln Ile Gln Asn Arg Ile Leu Leu Leu Phe Pro Lys | | | 864 |
| 275 | 280 | 285 | |
| ggg tcc cag tga | | | |
| Gly Ser Gln | | | 876 |
| 290 | | | |

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<211> 291
<212> PRT
<213> Homo sapiens

<400> 225

16U 200 PCT FINAL.ST25

| | | | | | | | | | | | | | | | |
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| Met | Tyr | Asn | Met | Ser | Asp | His | Gly | Thr | Gly | Leu | Phe | Ile | Leu | Leu | Gly |
| 1 | | | | | | | | 5 | 10 | | | | | | 15 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Pro | Gly | Leu | Glu | Gln | Tyr | His | Val | Trp | Ile | Ser | Ile | Pro | Phe | Cys |
| | | | | | | | | 20 | 25 | | | | | | 30 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Ile | Tyr | Leu | Met | Ala | Val | Val | Ala | Asn | Ser | Ile | Leu | Leu | Tyr | Leu |
| | | | | | | | | 35 | 40 | | | | | | 45 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| Ile | Val | Val | Glu | His | Ser | Leu | His | Ala | Pro | Met | Phe | Phe | Leu | Ser | |
| | | | | | | | | 50 | 55 | | | | | | 60 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Leu | Ala | Ile | Thr | Asp | Leu | Ile | Leu | Ser | Thr | Thr | Cys | Val | Pro | Lys |
| | | | | | | | | 65 | 70 | | | | | | 80 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Leu | Ser | Ile | Phe | Cys | Phe | Val | Leu | Asp | Ser | Ala | Ile | Leu | Leu | Ala |
| | | | | | | | | 85 | 90 | | | | | | 95 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Phe | Asp | Arg | Tyr | Met | Ala | Ile | Cys | Ser | Pro | Leu | Arg | Tyr | Thr |
| | | | | | | | | 100 | 105 | | | | | | 110 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Thr | Ile | Leu | Thr | Pro | Lys | Thr | Ile | Val | Lys | Ile | Ala | Val | Gly | Ile | Cys |
| | | | | | | | | 115 | 120 | | | | | | 125 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Phe | Arg | Ser | Phe | Cys | Val | Phe | Val | Pro | Cys | Val | Phe | Leu | Val | Asn | Arg |
| | | | | | | | | 130 | 135 | | | | | | 140 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Pro | Phe | Cys | Arg | Thr | His | Ile | Ile | Ser | His | Thr | Tyr | Cys | Glu | His |
| | | | | | | | | 145 | 150 | | | | | | 160 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Gly | Val | Ala | Gln | Leu | Ala | Cys | Ala | Asp | Ile | Ser | Ile | Asn | Ile | Trp |
| | | | | | | | | 165 | 170 | | | | | | 175 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Gly | Phe | Cys | Val | Pro | Ile | Met | Thr | Val | Met | Thr | Asp | Val | Ile | Leu |
| | | | | | | | | 180 | 185 | | | | | | 190 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Ala | Val | Ser | Tyr | Thr | Leu | Ile | Leu | Cys | Ala | Val | Phe | Cys | Leu | Pro |
| | | | | | | | | 195 | 200 | | | | | | 205 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Gln | Asp | Ala | Arg | Gln | Lys | Ala | Leu | Cys | Ser | Cys | Gly | Ser | His | Val |
| | | | | | | | | 210 | 215 | | | | | | 220 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cys | Val | Ile | Leu | Ile | Phe | Tyr | Ile | Pro | Ala | Phe | Phe | Ser | Ile | Leu | Ala |
| | | | | | | | | 225 | 230 | | | | | | 240 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| His | Cys | Phe | Gly | His | Asn | Val | Pro | His | Thr | Phe | His | Ile | Met | Phe | Ala |
| | | | | | | | | 245 | 250 | | | | | | 255 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Asn | Leu | Tyr | Val | Ile | Ile | Pro | Pro | Ala | Leu | Asn | Ser | Ile | Val | Tyr | Arg |
| | | | | | | | | 260 | 265 | | | | | | 270 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ile | Lys | Thr | Lys | Gln | Ile | Gln | Asn | Arg | Ile | Leu | Leu | Leu | Phe | Pro | Lys |
| | | | | | | | | 275 | 280 | | | | | | 285 |

| | | | | | | | | | | | | | | | |
|-----|-----|-----|--|--|--|--|--|--|--|--|--|--|--|--|-----|
| Gly | Ser | Gln | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | 290 |

<210> 226
<211> 1949
<212> DNA

16U 200 PCT FINAL.ST25

| | | |
|--|------|-----|
| Thr Ala Val Asn Leu Leu Ala Tyr Val Gly Asp Leu Val Tyr Ser Ala | | |
| 225 | 230 | 235 |
| cac ctg gtt ttt gtc aag gtc taagactccc aaagggccccc gttgcctct | 1194 | |
| His Leu Val Phe Val Lys Val | | |
| 240 | 245 | |
| ccaacctctt cattctgccc ccgctgagtt ttctttattt agtattcatt tcctgggtt | 1254 | |
| tcctctcccc tatctccctt cctccccc ttcttccttc ccaattcatc gcactttccc | 1314 | |
| agttctctga tgtatgttct tcccttctt ctgctgttcc ttcttgttt tgttctgtt | 1374 | |
| cccacaacct gtttcaccc gtttctttt ttccactctc tctttgtt cttcccttc | 1434 | |
| aattcttttc taggtttctt gtgggtttc ttatctgcct atttcccgac catcttctcc | 1494 | |
| tatccctgg ggagccctga ggctttctt ctctgcccc caagcaccc cagcgggtat | 1554 | |
| gagctccaca cccccacacc cattgcagct gtggcggccac gtcctccaa ggggccttct | 1614 | |
| gcccccccccc gccttagctg tgcccttagtc agtgtgtact tggtgtgtt tgggggagtg | 1674 | |
| ggaattgggc ccccttctc ccagtggagg aagggtgtct gtgcacccctc ccttaaatt | 1734 | |
| aaaaaaaaatg tatgtatctc tggaaagtcaa taattccag tgagcgggag gcttcaagcg | 1794 | |
| cagaccctgg gtccttagac ctcgccttgc actctgcctt gccagagatt ggctccagaa | 1854 | |
| tttgtgccag acttacagaa aacccactgc ctagaggcca tcttaaagga agcaatggat | 1914 | |
| ggatccctt catcccaact gttttcgcg gtatc | 1949 | |

<210> 227
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<212> PRT
<213> Homo sapiens

<400> 227

Met Thr Leu Val Ile Leu Leu Val Glu Leu Gly Ser Gln Ala Arg
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Phe Pro Leu Phe Trp Arg Asn Phe Pro Ile Thr Phe Ala Cys Tyr Ala
20 25 30

Ala Leu Leu Cys Leu Ser Ala Ser Ile Ile Tyr Pro Thr Thr Tyr Leu
35 40 45

Gln Phe Leu Ser His Gly Arg Ser Arg Asp His Ala Ile Ala Ala Ile
50 55 60

Val Phe Ser Gly Ile Ala Cys Val Ala Tyr Ala Thr Glu Val Thr Trp
65 70 75 80

Thr Arg Ala Arg Pro Gly Glu Ile Thr Asp Tyr Met Ala Ser Glu Leu
85 90 95

Gly Leu Leu Lys Val Leu Glu Thr Phe Val Ala Cys Leu Ile Phe Val
100 105 110

Phe Ile Asn Ser Pro Tyr Val Tyr His Asn Arg Pro Ala Leu Glu Trp
115 120 125

Trp Val Ala Val Tyr Ala Leu Cys Phe Val Leu Ala Ala Leu Thr Ile
130 135 140

Leu Leu Ser Leu Gly His Cys Thr Asn Met Leu Pro Ile Arg Phe Pro
145 150 155 160

160 200 PCT FINAL.ST25

Ser Phe Leu Leu Gly Leu Ala Leu Leu Ser Val Leu Leu Tyr Ala Thr
 165 170 175

Ala Leu Val Leu Trp Pro Leu Tyr Gln Phe Asn Glu Lys Tyr Gly Val
 180 185 190

Gln Pro Trp Gln Thr Arg Asp Val Ser Cys Ser Asp Arg Asn Pro Tyr
 195 200 205

Leu Val Cys Ile Trp Asp Arg Arg Leu Ala Val Thr Asn Leu Thr Ala
 210 215 220

Val Asn Leu Leu Ala Tyr Val Gly Asp Leu Val Tyr Ser Ala His Leu
 225 230 235 240

Val Phe Val Lys Val
 245

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 ctccggggcca gggtgacagg aggccgtgctt gagaggaaga agttgacggg aaggccagtg 180
 cgacggcaaa tctcgtgaac cttgggggac ga atg ctc agg atg cgg gtc ccc 233
 Met Leu Arg Met Arg Val Pro
 1 5

gcc ctc ctc gtc ctc ttc tgc ttc aga ggg aga gca ggc ccc tgc
 Ala Leu Leu Val Leu Phe Cys Phe Arg Gly Arg Ala Gly Pro Ser 281
 10 15 20

ccc cat ttc ctg caa cag cca gag gac ctg gtg ctg ctg ggg gag 329
 Pro His Phe Leu Gln Gln Pro Glu Asp Leu Val Val Leu Gly Glu
 25 30 35

gaa gcc cgg ctg ccc tgt gct ctg ggc gcc tac tgg ggg cta gtt cag 377
 Glu Ala Arg Leu Pro Cys Ala Leu Gly Ala Tyr Trp Gly Leu Val Gln
 40 45 50 55

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 60 65 70

tgg tcc cgg tac tgg ata tca ggg aat gca gcc aat ggc cag cat gac 473
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 75 80 85

ctc cac att agg ccc gtg gag cta gag gat gaa gca tca tat gaa tgt 521
 Leu His Ile Arg Pro Val Glu Leu Glu Asp Glu Ala Ser Tyr Glu Cys
 90 95 100

cag gct aca caa gca ggc ctc cgc tcc aga cca gcc caa ctg cac gtg 569
 Gln Ala Thr Gln Ala Gly Leu Arg Ser Arg Pro Ala Gln Leu His Val
 105 110 115

ctg gtc ccc cca gaa gcc ccc cag gtg ctg ggc ggc ccc tct gtg tct 617
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 120 125 130 135

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| | |
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| ggg ggc tct ccc gtg ctc ggg gcc cgc ggg cca agg tta gag gtc gtg Gly Gly Ser Pro Val Leu Gly Ala Arg Gly Pro Arg Leu Glu Val Val 265 270 275 | 1049 |
| gca gac gcc tcg ttc ctg act gag ccc gtg tcc tgc gag gtc agc aac Ala Asp Ala Ser Phe Leu Thr Glu Pro Val Ser Cys Glu Val Ser Asn 280 285 290 295 | 1097 |
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| ccg att ctg cag gca aag ccg gag ccc gtg tcc gtg gac gtg ggg gaa Pro Ile Leu Gln Ala Lys Pro Glu Pro Val Ser Val Asp Val Gly Glu 315 320 325 | 1193 |
| gac gct tcc ttc agc tgc gcc tgg cgc ggg aac ccg ctt cca ccg gta Asp Ala Ser Phe Ser Cys Ala Trp Arg Gly Asn Pro Leu Pro Arg Val 330 335 340 | 1241 |
| acc tgg acc cgc cgc ggt ggc gcg cag gtg ctg ggc tct gga gcc aca Thr Trp Thr Arg Arg Gly Gly Ala Gln Val Leu Gly Ser Gly Ala Thr 345 350 355 | 1289 |
| ctg cgt ctt ccg tcg gtg ggg ccc gag gac gca ggc gac tat gtg tgc Leu Arg Leu Pro Ser Val Gly Pro Glu Asp Ala Gly Asp Tyr Val Cys 360 365 370 375 | 1337 |
| * aga gct gag gct ggg cta tcg ggc ctg cgg ggc ggc gcc gct gag gct Arg Ala Glu Ala Gly Leu Ser Gly Leu Arg Gly Gly Ala Ala Glu Ala 380 385 390 | 1385 |
| cgg ctg act gtg aac gct ccc cca gta gtg acc gcc ctg cac tct gcg Arg Leu Thr Val Asn Ala Pro Pro Val Val Thr Ala Leu His Ser Ala 395 400 405 | 1433 |
| cct gcc ttc ctg agg ggc cct gct cgc ctc cag tgt ctg gtt ttc gcc Pro Ala Phe Leu Arg Gly Pro Ala Arg Leu Gln Cys Leu Val Phe Ala 410 415 420 | 1481 |
| tct ccc gcc cca gat ggc gtg gtc tgg tct tgg gat gag ggc ttc ctg Ser Pro Ala Pro Asp Ala Val Val Trp Ser Trp Asp Glu Gly Phe Leu 425 430 435 | 1529 |
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| cac agc aag gcc tca gcc tct ttc tcc gag caa aag aac ctg atg cga His Ser Lys Ala Ser Ala Ser Phe Ser Glu Gln Lys Asn Leu Met Arg 540 545 550 | 1865 |
| atc cct ggc agc agc gac ggc tcc agt tca cga ggt cct gaa gaa gag Ile Pro Gly Ser Ser Asp Gly Ser Ser Arg Gly Pro Glu Glu Glu 555 560 565 | 1913 |
| gag aca ggc agc cgc gag gac cgg ggc ccc att gtg cac act gac cac Glu Thr Gly Ser Arg Glu Asp Arg Gly Pro Ile Val His Thr Asp His 570 575 580 | 1961 |
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| ggc gaa gcc cct gga gga ggt ctc ttc ctg cca cca ccc tcc ccc ctt Gly Glu Ala Pro Gly Gly Leu Phe Leu Pro Pro Pro Ser Pro Leu 620 625 630 | 2105 |
| ggg ccc cca ggg acc cct acc ttc tat gac ttc aac cca cac ctg ggc Gly Pro Pro Gly Thr Pro Thr Phe Tyr Asp Phe Asn Pro His Leu Gly 635 640 645 | 2153 |
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| | | | | | | |
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| ccaaggagtg | gggatacagt | gagaattacc | actgttgggg | caaaatattg | ggataaaaat | 2946 |
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Gln Ala Leu Pro Thr Gly Arg Asp Thr Ala Ile Thr Leu Ser Leu Gln
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Gly Pro Arg Leu Glu Val Val Ala Asp Ala Ser Phe Leu Thr Glu Pro
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Ala Leu Asp Val Leu Phe Gly Pro Ile Leu Gln Ala Lys Pro Glu Pro
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Val Ala Leu Cys Cys Trp Arg His Ser Lys Ala Ser Ala Ser Phe Ser
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Met Leu Leu 895

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| ggg gac cta cac gta gac tgt gaa aaa aag ggc ttc aca agt ctg cag Gly Asp Leu His Val Asp Cys Glu Lys Lys Gly Phe Thr Ser Leu Gln 40 45 50 | 1039 |
| cgt ttc act gcc ccg act tcc cag ttt tac cat tta ttt ctg cat ggc Arg Phe Thr Ala Pro Thr Ser Gln Phe Tyr His Leu Phe Leu His Gly 55 60 65 | 1087 |
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| | | | | |
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| Ala Ile Ala Thr Gly Ser Ser Arg Asn Lys Pro Ala Asn Ser Leu | | | | |
| 325 | 330 | 335 | | |
| ccc tgc cct ggg ggc tgc agc tgc gac cac atc cca ggg tcg ggt tta | | | | 1951 |
| Pro Cys Pro Gly Gly Cys Ser Cys Asp His Ile Pro Gly Ser Gly Leu | | | | |
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| aag atg aac tgc aac aac agg aac gtg agc agc ttg gct gat ttg aag | | | | 1999 |
| Lys Met Asn Cys Asn Asn Arg Asn Val Ser Ser Leu Ala Asp Leu Lys | | | | |
| 360 | 365 | 370 | | |
| ccc aag ctc tct aac gtg cag gag ctt ttc cta cga gat aac aag atc | | | | 2047 |
| Pro Lys Leu Ser Asn Val Gln Glu Leu Phe Leu Arg Asp Asn Lys Ile | | | | |
| 375 | 380 | 385 | | |
| cac agc atc cga aaa tcg cac ttt gtg gat tac aag aac ctc att ctg | | | | 2095 |
| His Ser Ile Arg Lys Ser His Phe Val Asp Tyr Lys Asn Leu Ile Leu | | | | |
| 390 | 395 | 400 | | |
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| Leu Asp Leu Gly Asn Asn Ile Ala Thr Val Glu Asn Asn Thr Phe | | | | |
| 405 | 410 | 415 | | |
| aag aac ctt ttg gac ctc agg tgg cta tac atg gat agc aat tac ctg | | | | 2191 |
| Lys Asn Leu Leu Asp Leu Arg Trp Leu Tyr Met Asp Ser Asn Tyr Leu | | | | |
| 420 | 425 | 430 | 435 | |
| gac acg ctg tcc cgg gag aaa ttc gcg ggg ctg caa aac cta gag tac | | | | 2239 |
| Asp Thr Leu Ser Arg Glu Lys Phe Ala Gly Leu Gln Asn Leu Glu Tyr | | | | |
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| 455 | 460 | 465 | | |
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| Asn Ala Met Pro Lys Leu Arg Ile Leu Ile Leu Asn Asn Asn Leu Leu | | | | |
| 470 | 475 | 480 | | |
| agg tcc ctg cct gtg gac gtg ttc gct ggg gtc tcg ctc tct aaa ctc | | | | 2383 |
| Arg Ser Leu Pro Val Asp Val Phe Ala Gly Val Ser Leu Ser Lys Leu | | | | |
| 485 | 490 | 495 | | |
| agc ctg cac aac aat tac ttc atg tac ctc ccg gtg gca ggg gtg ctg | | | | 2431 |
| Ser Leu His Asn Asn Tyr Phe Met Tyr Leu Pro Val Ala Gly Val Leu | | | | |
| 500 | 505 | 510 | 515 | |
| gac cag tta acc tcc atc atc cag ata gac ctc cac gga aac ccc tgg | | | | 2479 |
| Asp Gln Leu Thr Ser Ile Ile Gln Ile Asp Leu His Gly Asn Pro Trp | | | | |
| 520 | 525 | 530 | | |
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| Glu Cys Ser Cys Thr Ile Val Pro Phe Lys Gln Trp Ala Glu Arg Leu | | | | |
| 535 | 540 | 545 | | |
| ggc tcc gaa gtg ctg atg agc gac ctc aag tgt gag acg ccg gtg aac | | | | 2575 |
| Gly Ser Glu Val Leu Met Ser Asp Leu Lys Cys Glu Thr Pro Val Asn | | | | |
| 550 | 555 | 560 | | |
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| 565 | 570 | 575 | | |
| cag ctg tac gct agg atc tcg ccc acg tta act tcg cac agt aaa aac | | | | 2671 |
| Gln Leu Tyr Ala Arg Ile Ser Pro Thr Leu Thr Ser His Ser Lys Asn | | | | |
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| 600 | 605 | 610 | | |
| acc agc agg gtg tcc atc tcg gtg ttg gtc ccg gga ctg ctg ctg gtg | | | | 2767 |
| Thr Ser Arg Val Ser Ile Ser Val Leu Val Pro Gly Leu Leu Val | | | | |
| 615 | 620 | 625 | | |

| | |
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| gag att aat tcc cta cag aca gtc tgt gac tct tcc tac tgg cac aat Glu Ile Asn Ser Leu Gln Thr Val Cys Asp Ser Ser Tyr Trp His Asn 660 665 670 675 | 2911 |
| ggg cct tac aac gca gat ggg gcc cac aga gtg tat gac tgt ggc tct Gly Pro Tyr Asn Ala Asp Gly Ala His Arg Val Tyr Asp Cys Gly Ser 680 685 690 | 2959 |
| cac tcg ctc tca gac taagacccca accccaatag gggagggcag agggaaaggcg His Ser Leu Ser Asp 695 | 3014 |
| atacatcctt ccccacccgca ggcaccccg gggctggagg ggcgtgtacc caaatccccg cgccatcagc ctggatgggc ataagttagat aaataactgt gagctcgcac aaccgaaaagg gcctgacccc ttacttagct ccctccttga aacaaagagc agactgtgga gagctggag agcgcagcca gtcgctctt tgctgagagc ccctttgac agaaagccca gcacgaccct gctgaaagaa ctgacagtgc cctcgccctc ggccccgggg cctgtggggt tggatgccgc ggttctatac atatatacat atatccacat ctatata>tagag agatagatat ctattttcc cctgtggatt agcccggtga tggtccctg ttggctacgc agggatgggc agttgcacga aggcatgaat gtattgtaaa taagtaactt tgacttctga caaaaaacaa aaagtgcgtc atggctcgca tggaatccac ggcgtccagg gactctgccc gccccgcga ctggagacgg catctcggtt acagcaccca ccctcttacc tgataagttt catcgatata aactttctat aaacaaaata cagtataatc agaaaagtgc atttcgccat tatttgtat cggtaggcag ttcagagcat aagttactg tgaaaaaaat gtaaaagggtt tatttaggac atttgcattgg ctagtcata gtcattttta tgagttaca atgtatggg ttgagggaaag ttttttaggg ttgtttggg ttcttttatt ttgatggtga tgttttatatt tattttatatt ttttcagggg gtctttttt taatacatat ccaataatgc cttccatctg aatgtaaaat aagtaccat gatttctatt atagtatcatg tgtaattttt taaaatgtaa ttttgaggca gtttagcatg accaattaat gtcactctag tgcttaggct ggcgtccat ggttagcaatt ctgtgctgg ataaaatcttta cttataaagt agggaaaagag aaccgaggaa gcacgtgaaa cttactaatt ctattcgagg attttataat ggcataatttt ttcatgtat aagcgaaaat gttttcaact ctgggtcctt accttttcc acgttccatat ttgcaagtgg taaattggat ttgcgggtgg -agagacaggg gagggaaacg gttgggtta gatcccttcc tgagctacat taaggcttt tctctaattcg cttctacttag ctttttaccc ttaagtagc tccttccccc tcgccccac cctctacccc accccaccc tgcgtcagac ttaccggct ttcccagtc cataaaggtc ttgccccaaac actccccct tcttttttc ccctctccaa atgcagcgt gaatccctt attaatactg gaaatccctc tctgtgttt ttgttgtgc tgcccacact gcagatata taaggatgtt aggagagatt tgattnaatt gactctgcct agataggctt cattaaacag agtggagatt tcattggtca gcaactcctca atgaaagaca gacctaattga ctggcattt agatgctgct ggcattttga attcaacatc tgctgaaaac ggtaaaaacta attagtcccc acccacccctc cccgccccag caactgcata ttgaaattt gtaaagcact catctttatg gaaattnaattc attatcctaa agaagtgttt ctctccatc atccggattt ctgggttgtgg 4814 | 3074 3134 3194 3254 3314 3374 3434 3494 3554 3614 3674 3734 3794 3854 3914 3974 4034 4094 4154 4214 4274 4334 4394 4454 4514 4574 4634 4694 4754 |

16U 200 PCT FINAL.ST25

| | | | | | | |
|------------|--------------|------------|------------|------------|-------------|------|
| cccagcaatt | aacaaaaaca | gcttcaactg | tgcgaattt | atgaaccaat | gtaaactctgg | 4874 |
| cctcaatcat | attcctctgg | gatttctaaa | cagcagttaa | gctacaaaaa | gcaaacaaaa | 4934 |
| ccacacatat | tgcattggagtc | tgcattccac | cacatatcca | cccttgagaa | gtatgtcaaa | 4994 |
| agactgcaga | ctatagattt | tttttaata | taggattata | aatcagctag | tgaaagacct | 5054 |
| cagaggagtt | gtaaatgtat | ctgccatcta | gaactcatat | tctaaaggga | agtgattct | 5114 |
| cagaacagtg | atgttctgga | atatgtatta | tttattttaa | cacttttta | ataaaatctt | 5174 |
| tattataaac | catg | | | | | 5188 |

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<400> 231

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20 25 30

Glu Ile Glu Gly Asp Leu His Val Asp Cys Glu Lys Lys Gly Phe Thr
35 40 45

Ser Leu Gln Arg Phe Thr Ala Pro Thr Ser Gln Phe Tyr His Leu Phe
50 55 60

Leu His Gly Asn Ser Leu Thr Arg Leu Phe Pro Asn Glu Phe Ala Asn
65 70 75 80

Phe Tyr Asn Ala Val Ser Leu His Met Glu Asn Asn Gly Leu His Glu
85 90 95

Ile Val Pro Gly Ala Phe Leu Gly Leu Gln Leu Val Lys Arg Leu His
100 105 110

Ile Asn Asn Asn Lys Ile Lys Ser Phe Arg Lys Gln Thr Phe Leu Gly
115 120 125

Leu Asp Asp Leu Glu Tyr Leu Gln Ala Asp Phe Asn Leu Leu Arg Asp
130 135 140

Ile Asp Pro Gly Ala Phe Gln Asp Leu Asn Lys Leu Glu Val Leu Ile
145 150 155 160

Leu Asn Asp Asn Leu Ile Ser Thr Leu Pro Ala Asn Val Phe Gln Tyr
165 170 175

Val Pro Ile Thr His Leu Asp Leu Arg Gly Asn Arg Leu Lys Thr Leu
180 185 190

Pro Tyr Glu Glu Val Leu Glu Gln Ile Pro Gly Ile Ala Glu Ile Leu
195 200 205

Leu Glu Asp Asn Pro Trp Asp Cys Thr Cys Asp Leu Leu Ser Leu Lys
210 215 220

160 200 PCT FINAL.ST25

| | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Glu | Trp | Leu | Glu | Asn | Ile | Pro | Lys | Asn | Ala | Leu | Ile | Gly | Arg | Val | Val |
| 225 | | | | | | 230 | | | | 235 | | | | | 240 |

Cys Glu Ala Pro Thr Arg Leu Gln Gly Lys Asp Leu Asn Glu Thr Thr
245 250 255

Glu Gln Asp Leu Cys Pro Leu Lys Asn Arg Val Asp Ser Ser Leu Pro
260 265 270

Ala Pro Pro Ala Gln Glu Glu Thr Phe Ala Pro Gly Pro Leu Pro Thr
275 280 285

Pro Phe Lys Thr Asn Gly Gln Glu Asp His Ala Thr Pro Gly Ser Ala
290 295 300

Pro Asn Gly Gly Thr Lys Ile Pro Gly Asn Trp Gln Ile Lys Ile Arg
305 310 315 320

Pro Thr Ala Ala Ile Ala Thr Gly Ser Ser Arg Asn Lys Pro Leu Ala
325 330 335

Asn Ser Leu Pro Cys Pro Gly Gly Cys Ser Cys Asp His Ile Pro Gly
340 345 350

Ser Gly Leu Lys Met Asn Cys Asn Asn Arg Asn Val Ser Ser Leu Ala
355 360 365

Asp Leu Lys Pro Lys Leu Ser Asn Val Gln Glu Leu Phe Leu Arg Asp
370 375 380

Asn Lys Ile His Ser Ile Arg Lys Ser His Phe Val Asp Tyr Lys Asn
385 390 395 400

Leu Ile Leu Leu Asp Leu Gly Asn Asn Ile Ala Thr Val Glu Asn
405 410 415

Asn Thr Phe Lys Asn Leu Leu Asp Leu Arg Trp Leu Tyr Met Asp Ser
420 425 430

Asn Tyr Leu Asp Thr Leu Ser Arg Glu Lys Phe Ala Gly Leu Gln Asn
435 440 445

Leu Glu Tyr Leu Asn Val Glu Tyr Asn Ala Ile Gln Leu Ile Leu Pro
450 455 460

-Gly Thr Phe Asn Ala Met Pro Lys Leu Arg Ile Leu Ile Leu Asn Asn
465 470 475 480

Asn Leu Leu Arg Ser Leu Pro Val Asp Val Phe Ala Gly Val Ser Leu
485 490 495

Ser Lys Leu Ser Leu His Asn Asn Tyr Phe Met Tyr Leu Pro Val Ala
500 505 510

Gly Val Leu Asp Gln Leu Thr Ser Ile Ile Gln Ile Asp Leu His.Gly
515 520 525

Asn Pro Trp Glu Cys Ser Cys Thr Ile Val Pro Phe Lys Gln Trp Ala
530 535 540

16U 200 PCT FINAL.ST25

Glu Arg Leu Gly Ser Glu Val Leu Met Ser Asp Leu Lys Cys Glu Thr
 545 550 555 560

Pro Val Asn Phe Phe Arg Lys Asp Phe Met Leu Leu Ser Asn Asp Glu
 565 570 575

Ile Cys Pro Gln Leu Tyr Ala Arg Ile Ser Pro Thr Leu Thr Ser His
 580 585 590

Ser Lys Asn Ser Thr Gly Leu Ala Glu Thr Gly Thr His Ser Asn Ser
 595 600 605

Tyr Leu Asp Thr Ser Arg Val Ser Ile Ser Val Leu Val Pro Gly Leu
 610 615 620

Leu Leu Val Phe Val Thr Ser Ala Phe Thr Val Val Gly Met Leu Val
 625 630 635 640

Phe Ile Leu Arg Asn Arg Lys Arg Ser Lys Arg Arg Asp Ala Asn Ser
 645 650 655

Ser Ala Ser Glu Ile Asn Ser Leu Gln Thr Val Cys Asp Ser Ser Tyr
 660 665 670

Trp His Asn Gly Pro Tyr Asn Ala Asp Gly Ala His Arg Val Tyr Asp
 675 680 685

Cys Gly Ser His Ser Leu Ser Asp
 690 695

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<211> 506
<212> DNA
<213> Homo sapiens

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<222> (32)..(346)
<223>

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Met Ala Lys Met Phe Asp Leu
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agg acg aag atc atc ggc atc gga agc agc tta ctg gtt gcc gcg 100
Arg Thr Lys Ile Met Ile Gly Ile Gly Ser Ser Leu Leu Val Ala Ala
10 15 20

atg gtg ctc cta agt gtt gtg ttc tgt ctt tac ttc aaa gta gct aag 148
Met Val Leu Leu Ser Val Val Phe Cys Leu Tyr Phe Lys Val Ala Lys
25 30 35

gca cta aaa gct gca aag gac cct gat gct gtg gct gta aaa aat cac 196
Ala Leu Lys Ala Ala Lys Asp Pro Asp Ala Val Ala Val Lys Asn His
40 45 50 55

aac cca gac aag gtg tgt tgg gcc acg aac agc cag gcc aaa gcc acc 244
Asn Pro Asp Lys Val Cys Trp Ala Thr Asn Ser Gln Ala Lys Ala Thr
60 65 70

acc atg gag tct tgt cca tct ctc cag tgc tgt gaa ggt tgt aga atg 292
Thr Met Glu Ser Cys Pro Ser Leu Gln Cys Cys Glu Gly Cys Arg Met
75 80 85

cat gcc agt tct gat tcc ctg cca cct tgc tgt gac ata aat gag 340
His Ala Ser Ser Asp Ser Leu Pro Pro Cys Cys Cys Asp Ile Asn Glu
90 95 100

16U 200 PCT FINAL.ST25

ggc ctc tgaacttggga aagctggca caaaaatctt catgagcaat atttctttct 396
 Gly Leu
 105

taatagaatg ttttattttt caagtcaagt tcttaggtgt ttacatacta ttatataatg 456
 tacagtgtta tttctgtac ttctgaataa atgtgcaata tgaaataa 506

<210> 233
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 <213> Homo sapiens

<400> 233

Met Ala Lys Met Phe Asp Leu Arg Thr Lys Ile Met Ile Gly Ile Gly
 1 5 10 15

Ser Ser Leu Leu Val Ala Ala Met Val Leu Leu Ser Val Val Phe Cys
 20 25 30

Leu Tyr Phe Lys Val Ala Lys Ala Leu Lys Ala Ala Lys Asp Pro Asp
 35 40 45

Ala Val Ala Val Lys Asn His Asn Pro Asp Lys Val Cys Trp Ala Thr
 50 55 60

Asn Ser Gln Ala Lys Ala Thr Thr Met Glu Ser Cys Pro Ser Leu Gln
 65 70 75 80

Cys Cys Glu Gly Cys Arg Met His Ala Ser Ser Asp Ser Leu Pro Pro
 85 90 95

Cys Cys Cys Asp Ile Asn Glu Gly Leu
 100 105

<210> 234
 <211> 1037
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (180)...(560)
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<400> 234
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aaccggaaat accaaaggat tatctccaat attccagggc cttctttctc atctctgtct 120

-ttaccatact tactggcctt ggctggctct tcagctcttg gatccttaat cgaggaagc 179

atg acc acc aac ttg gat ctg aag gta tcc atg ctc agc ttc atc tca 227
 Met Thr Asn Leu Asp Leu Lys Val Ser Met Leu Ser Phe Ile Ser
 1 5 10 15

gct acc tgc ttg ctc ctc tgc aac ctg ttt gtg gca cag gtt cac 275
 Ala Thr Cys Leu Leu Leu Cys Leu Asn Leu Phe Val Ala Gln Val His
 20 25 30

tgg cat act agg gat gcc atg gag tca gat ctc cta tgg acc tat tat 323
 Trp His Thr Arg Asp Ala Met Glu Ser Asp Leu Leu Trp Thr Tyr Tyr
 35 40 45

ctt aac tgg tgc aqt gac atc ttt tac atg ttt gct ggg atc atc tct 371
 Leu Asn Trp Cys Ser Asp Ile Phe Tyr Met Phe Ala Gly Ile Ile Ser
 50 55 60

ctt ctc aac tac tta act tcc aga tcg cct gcc tgt gat gaa aac gtc 419

16U 200 PCT FINAL.ST25

| | | | |
|--|-----|------|----|
| Leu Leu Asn Tyr Leu Thr Ser Arg Ser Pro Ala Cys Asp Glu Asn Val | | | |
| 65 | 70 | 75 | 80 |
| act gtg att cca aca gag aga tca agg ctg ggg gtt ggt ccg gtg act | | 467 | |
| Thr Val Ile Pro Thr Glu Arg Ser Arg Leu Gly Val Gly Pro Val Thr | | | |
| 85 | 90 | 95 | |
| aca gta tca cct gct aaa gat gaa ggg cca agg tct gag atg gaa tct | | 515 | |
| Thr Val Ser Pro Ala Lys Asp Glu Gly Pro Arg Ser Glu Met Glu Ser | | | |
| 100 | 105 | 110 | |
| cta agt gtg aga gag aaa aat tta cca aag tca gga ctg tgg tgg | | 560 | |
| Leu Ser Val Arg Glu Lys Asn Leu Pro Lys Ser Gly Leu Trp Trp | | | |
| 115 | 120 | 125 | |
| tgtataggaaa acctaactat agcttgctt aaaagcagg gagaagctga gttggaaatg | | 620 | |
| gtcacataaa ttctggaaat ctctccataat atcatgtcca tattacttga ggagacagca | | 680 | |
| ttaaaagctga tgaatgtct ttgcgtgca ttggatccaa aatatataatg atagtataaa | | 740 | |
| agtaaataaac tcacttaaga aaaacatttc taaaagaaaa caacaatgtt tagagtcatg | | 800 | |
| aatgaaagaa actagtgaaa gatgcagtgt gtagaccaga gacctcttg ggtatcagg | | 860 | |
| atctcatgga ccagaatggc ccgtggagaa gaatgttaat tacttctgtt tggaaatttc | | 920 | |
| tttattatgt gtggcttgg gtatactcag gatggaaagc acttggacaa atactgttga | | 980 | |
| atctgaacctt aatagcatta ccagaaatgg aataaatatc aatggatata agaccta | | 1037 | |

<210> 235

<211> 127

<212> PRT

<213> Homo sapiens

<400> 235

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| Met Thr Thr Asn Leu Asp Leu Lys Val Ser Met Leu Ser Phe Ile Ser | | | |
| 1 | 5 | 10 | 15 |

| | | |
|---|----|----|
| Ala Thr Cys Leu Leu Cys Leu Asn Leu Phe Val Ala Gln Val His | | |
| 20 | 25 | 30 |

| | | |
|---|----|----|
| Trp His Thr Arg Asp Ala Met Glu Ser Asp Leu Leu Trp Thr Tyr Tyr | | |
| 35 | 40 | 45 |

| | | |
|---|----|----|
| Leu Asn Trp Cys Ser Asp Ile Phe Tyr Met Phe Ala Gly Ile Ile Ser | | |
| 50 | 55 | 60 |

| | | | |
|---|----|----|----|
| Leu Leu Asn Tyr Leu Thr Ser Arg Ser Pro Ala Cys Asp Glu Asn Val | | | |
| 65 | 70 | 75 | 80 |

| | | |
|---|----|----|
| Thr Val Ile Pro Thr Glu Arg Ser Arg Leu Gly Val Gly Pro Val Thr | | |
| 85 | 90 | 95 |

| | | |
|---|-----|-----|
| Thr Val Ser Pro Ala Lys Asp Glu Gly Pro Arg Ser Glu Met Glu Ser | | |
| 100 | 105 | 110 |

| | | |
|---|-----|-----|
| Leu Ser Val Arg Glu Lys Asn Leu Pro Lys Ser Gly Leu Trp Trp | | |
| 115 | 120 | 125 |

<210> 236

<211> 1054

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (152)..(895)

16U 200 PCT FINAL.ST25

<223>

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|---|------|--|
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| gttggcattc ggtggccctg gcagtttagct gagcacgc ctc tctgagccgc tcgggtggaca | 60 | |
| ccaggcaactc tagtaggcct ggccatccccaa gaaacagcag gagagagaag aaacaggcca | 120 | |
| gctgtgagaa gccaaaggaca ccgagtcagt c atg gca cct aag gcg gca aag Met Ala Pro Lys Ala Ala Lys | 172 | |
| 1 5 | | |
| ggg gcc aag cca gag cca gca cca gct cca cct cca ccc ggg gcc aaa Gly Ala Lys Pro Glu Pro Ala Pro Ala Pro Pro Pro Gly Ala Lys | 220 | |
| 10 15 20 | | |
| ccc gag gaa gac aag aag gac ggt aag gag cca tcg gac aaa cct caa Pro Glu Glu Asp Lys Lys Asp Gly Lys Glu Pro Ser Asp Lys Pro Gln | 268 | |
| 25 30 35 | | |
| aag gcg gtg cag gac cat aag gag cca tcg gac aaa cct caa aag gcg Lys Ala Val Gln Asp His Lys Glu Pro Ser Asp Lys Pro Gln Lys Ala | 316 | |
| 40 45 50 55 | | |
| gtg cag ccc aag cac gaa gtg ggc acg agg agg ggg tgt cgc cgc tac Val Gln Pro Lys His Glu Val Gly Thr Arg Arg Gly Cys Arg Arg Tyr | 364 | |
| 60 65 70 | | |
| cgg tgg gaa tta aaa gac agc aat aaa gag ttc tgg ctc ttg ggg cac Arg Trp Glu Leu Lys Asp Ser Asn Lys Glu Phe Trp Leu Leu Gly His | 412 | |
| 75 80 85 | | |
| gct gag atc aag att cgg agt ttg ggc tgc cta ata gct gca atg ata Ala Glu Ile Lys Ile Arg Ser Leu Gly Cys Leu Ile Ala Ala Met Ile | 460 | |
| 90 95 100 | | |
| ctg ttg tcc tca ctc acc gtg cac ccc atc ttg agg ctt atc atc acc Leu Leu Ser Ser Leu Thr Val His Pro Ile Leu Arg Leu Ile Ile Thr | 508 | |
| 105 110 115 | | |
| atg gag ata tcc ttc ttc agc ttc atc tta ctg tac agc ttt gcc Met Glu Ile Ser Phe Ser Phe Phe Ile Leu Leu Tyr Ser Phe Ala | 556 | |
| 120 125 130 135 | | |
| att cat aga tac ata ccc ttc atc ctg tgg ccc att tct gac ctc ttc Ile His Arg Tyr Ile Pro Phe Ile Leu Trp Pro Ile Ser Asp Leu Phe | 604 | |
| 140 145 150 | | |
| aac gac ctg att gct tgt gcg ttc ctt gtg gga gcc gtg gtc ttt gct Asn Asp Leu Ile Ala Cys Ala Phe Leu Val Gly Ala Val Val Phe Ala | 652 | |
| 155 160 165 | | |
| gtg aga agt cgg cga tcc atg aat ctc cac tac tta ctt gct gtg atc Val Arg Ser Arg Arg Ser Met Asn Leu His Tyr Leu Leu Ala Val Ile | 700 | |
| 170 175 180 | | |
| ctt att ggt gcg gct gga gtt ttt gct ttt atc gat gtg tgt ctt caa Leu Ile Gly Ala Ala Gly Val Phe Ala Phe Ile Asp Val Cys Leu Gln | 748 | |
| 185 190 195 | | |
| aga aac cac ttc aga ggc aag aag gcc aaa aag cat atg ctg gtt cct -Arg Asn His Phe Arg Gly Lys Lys Ala Lys Lys His Met Leu Val Pro | 796 | |
| 200 205 210 215 | | |
| cct cca gga aag gaa aaa gga ccc cag cag ggc aag gga cca gaa ccc Pro Pro Gly Lys Gly Pro Gln Gln Gly Lys Gly Pro Glu Pro | 844 | |
| 220 225 230 | | |
| gcc aag cca cca gaa cct ggc aag cca cca ggg cca gca aag gga aag Ala Lys Pro Pro Glu Pro Gly Lys Pro Pro Gly Pro Ala Lys Gly Lys | 892 | |
| 235 240 245 | | |
| aaa tgacttggag gaggctccctg gtgtctgaaa cggcagtgtatttacagca Lys | 945 | |
| atatgtttcc actctttcc ttgtcttctt tctggaatgg ttttcttttc cattttcatt | 1005 | |
| accaccccttg cttggaaaag aatggattcaa tggattctaa aagcctaaa | 1054 | |

16U 200 PCT FINAL.ST25

<210> 237
<211> 248
<212> PRT
<213> Homo sapiens

<400> 237

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Pro Pro Pro Pro Gly Ala Lys Pro Glu Glu Asp Lys Lys Asp Gly Lys
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Glu Pro Ser Asp Lys Pro Gln Lys Ala Val Gln Asp His Lys Glu Pro
35 40 45

Ser Asp Lys Pro Gln Lys Ala Val Gln Pro Lys His Glu Val Gly Thr
50 55 60

Arg Arg Gly Cys Arg Arg Tyr Arg Trp Glu Leu Lys Asp Ser Asn Lys
65 70 75 80

Glu Phe Trp Leu Leu Gly His Ala Glu Ile Lys Ile Arg Ser Leu Gly
85 90 95

Cys Leu Ile Ala Ala Met Ile Leu Leu Ser Ser Leu Thr Val His Pro
100 105 110

Ile Leu Arg Leu Ile Ile Thr Met Glu Ile Ser Phe Phe Ser Phe Phe
115 120 125

Ile Leu Leu Tyr Ser Phe Ala Ile His Arg Tyr Ile Pro Phe Ile Leu
130 135 140

Trp Pro Ile Ser Asp Leu Phe Asn Asp Leu Ile Ala Cys Ala Phe Leu
145 150 155 160

Val Gly Ala Val Val Phe Ala Val Arg Ser Arg Arg Ser Met Asn Leu
165 170 175

His Tyr Leu Leu Ala Val Ile Leu Ile Gly Ala Ala Gly Val Phe Ala
180 185 190

Phe Ile Asp Val Cys Leu Gln Arg Asn His Phe Arg Gly Lys Lys Ala
195 200 205

Lys Lys His Met Leu Val Pro Pro Pro Gly Lys Glu Lys Gly Pro Gln
210 215 220

Gln Gly Lys Gly Pro Glu Pro Ala Lys Pro Pro Glu Pro Gly Lys Pro
225 230 235 240

Pro Gly Pro Ala Lys Gly Lys Lys
245

<210> 238
<211> 487
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<213> Homo sapiens

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16U 200 PCT FINAL.ST25

<222> (17)..(418)
<223>

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 1 5 10

ctt ctg ctg ttg ctt agc aac tgg ttg gtc aag tat gaa cac aag ctc 100
 Leu Leu Leu Leu Ser Asn Trp Leu Val Lys Tyr Glu His Lys Leu
 15 20 25

acc ctc cca gag ccc cag cag gag gaa gag aaa cca aag act tct gaa 148
 Thr Leu Pro Glu Pro Gln Gln Glu Glu Glu Lys Pro Lys Thr Ser Glu
 30 35 40

aac gac tcc aag aac agc aag gcc gtg aac aca aaa gaa gtc aat aga 196
 Asn Asp Ser Lys Asn Ser Lys Ala Val Asn Thr Lys Glu Val Asn Arg
 45 50 55 60

acg cat gcc tgc ttt gcc ctc cag gac gag atc ctc caa cgg ctg ttg 244
 Thr His Ala Cys Phe Ala Leu Gln Asp Glu Ile Leu Gln Arg Leu Leu
 65 70 75

tcc aat gaa atg aag atg aag gtc cta gaa aat cag atg ttc atc ata 292
 Phe Ser Glu Met Lys Met Lys Val Leu Glu Asn Gln Met Phe Ile Ile
 80 85 90

tgg aat aaa atg aat cac cac ggg cgg tca agc aga cat cgg aat ttt 340
 Trp Asn Lys Met Asn His His Gly Arg Ser Ser Arg His Arg Asn Phe
 95 100 105

ccc atg aaa aaa cac aga atg agg agg cat gag tca att tgc ccc acc 388
 Pro Met Lys Lys His Arg Met Arg Arg His Glu Ser Ile Cys Pro Thr
 110 115 120

ctg tct gac tgt act tcg aat tcc ccc agc taatgaggcc gaggcggtct 438
 Leu Ser Asp Cys Thr Ser Ser Pro Ser
 125 130

ggcctctgcc gatgttacct ttacccat taaaacccag tcacagcct 487

<210>. 239

<211> 134

<212> PRT

<213> Homo sapiens

<400> 239

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 1 5 10 15

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 20 25 30

Pro Gln Gln Glu Glu Lys Pro Lys Thr Ser Glu Asn Asp Ser Lys
 35 40 45

Asn Ser Lys Ala Val Asn Thr Lys Glu Val Asn Arg Thr His Ala Cys
 50 55 60

Phe Ala Leu Gln Asp Glu Ile Leu Gln Arg Leu Leu Phe Ser Glu Met
 65 70 75 80

Lys Met Lys Val Leu Glu Asn Gln Met Phe Ile Ile Trp Asn Lys Met
 85 90 95

Asn His His Gly Arg Ser Ser Arg His Arg Asn Phe Pro Met Lys Lys
 100 105 110

His Arg Met Arg Arg His Glu Ser Ile Cys Pro Thr Leu Ser Asp Cys

115 120 16U 200 PCT FINAL ST25
125

Thr Ser Ser Ser Pro Ser
130

<210> 240
<211> 846
<212> DNA
<213> *Homo sapiens*

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<222> (108)..(725)
<223>

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agttccctct ccccagagcc atcggccagg taccaaagct cagctgt atg gat tcc 116
Met Asp Ser
1

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caa cag gag gac ctg cgc ttc cct ggg atg tgg gtc tca ttg tac ttt      164
Gln Gln Glu Asp Leu Arg Phe Pro Gly Met Trp Val Ser Leu Tyr Phe
      5          10           15

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| | |
|---|-----|
| gga atc ctg ggg ctg tgt tct gtg ata act gga ggg tgc att atc tt | 212 |
| Gly Ile Leu Gly Leu Cys Ser Val Ile Thr Gly Gly Cys Ile Ile Phe | |
| 20 25 30 35 | |

ctg cac tgg agg aag aac ttg agg cgg gaa gag cat gcc cag cag tgg 260
 Leu His Trp Arg Lys Asn Leu Arg Arg Glu Glu His Ala Gln Gln Trp
 40 45 50

| | | |
|---|-----|----|
| gtg gag gtg atg aga gct gcc aca ttc acc tac agc cca ttg ttg tac | 308 | |
| Val Glu Val Met Arg Ala Ala Thr Phe Thr Tyr Ser Pro Leu Leu Tyr | | |
| 55 | 60 | 65 |

tgg att aac aag cga cgg cgc tac ggc atg aat gca gcc atc aac acg 356
Trp Ile Asn Lys Arg Arg Arg Tyr Gly Met Asn Ala Ala Ile Asn Thr
70 75 80

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Gly Pro Ala Pro Ala Val Thr Lys Thr Glu Thr Glu Val Gln Asn Pro
     85          90          95

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| | |
|---|-----|
| gat gtt ctg tgg gat ttg gac atc ccc gaa ggc agg agc cat gct gac | 452 |
| Asp Val Leu Trp Asp Leu Asp Ile Pro Glu Gly Arg Ser His Ala Asp | |
| 100 105 110 115 | |

caa gac agc aac ccc aag gcg gaa gcc cct gct ccc ctg caa cct gca 500
 Gln Asp Ser Asn Pro Lys Ala Glu Ala Pro Ala Pro Leu Gln Pro Ala
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ctg cag ctg gct cca cag cag ccc cag gcc aga tcc cca ttc cca ctt 548
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 135 140 145

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 Pro Ile Phe Gln Glu Val Pro Phe Ala Pro Pro Leu Cys Asn Leu Pro
    150          155          160

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ccc ctg ctg aac cac tct gtc tcc tat cct ttg gcc acc tgt cct gaa 644
 Pro Leu Leu Asn His Ser Val Ser Tyr Pro Leu Ala Thr Cys Pro Glu
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Arg Asn Val Leu Phe His Ser Leu Leu Asp Leu Ala Gln Glu Asp His

180 185 190 195
agc ttc aat gcc aag cct ttt cct tca gaa ctg tagcctccctc tcactgaagg 745
Ser Phe Asn Glu Pro Lys Pro Phe Pro Ser Glu Ile

tgggagctgc aggaatcagg tgcagagtag gaaatggAAC taactcagg aaggTggtat 805

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35 40 45

Gln Gln Trp Val Glu Val Met Arg Ala Ala Thr Phe Thr Tyr Ser Pro
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Leu Leu Tyr Trp Ile Asn Lys Arg Arg Arg Tyr Gly Met Asn Ala Ala
65 70 75 80

Ile Asn Thr Gly Pro Ala Pro Ala Val Thr Lys Thr Glu Thr Glu Val
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Gln Asn Pro Asp Val Leu Trp Asp Leu Asp Ile Pro Glu Gly Arg Ser
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His Ala Asp Gln Asp Ser Asn Pro Lys Ala Glu Ala Pro Ala Pro Leu
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Phe Pro Leu Pro Ile Phe Gln Glu Val Pro Phe Ala Pro Pro Leu Cys
145 150 155 160

Asn Leu Pro Pro Leu Leu Asn His Ser Val Ser Tyr Pro Leu Ala Thr
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Asp Asn Leu Leu Glu Ser Leu Ser Thr Val Trp Asn Trp Ile
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16U 200 PCT FINAL.ST25

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 Gly Leu Leu Asp Asn Leu Ala Pro Ala Val Gln Ile Ile Leu Arg Ile
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 tct ttc ttg att tta ttg gga ata gga ata tat gcc tta tgg aaa cga 246
 Ser Phe Leu Ile Leu Leu Gly Ile Gly Ile Tyr Ala Leu Trp Lys Arg
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 agt att cag tca att cag aaa aca ttg ttg ttt gta atc aca ctc tac 294
 Ser Ile Gln Ser Ile Gln Lys Thr Leu Leu Phe Val Ile Thr Leu Tyr
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 aaa ctt tac aag aag ggc tca cat att ttt gag gct ttg cta gcc aac 342
 Lys Leu Tyr Lys Gly Ser His Ile Phe Glu Ala Leu Leu Ala Asn
 90 95 100

 cca gaa gga agt ggt ctc cga att caa gac aat aat aat ctt ttc ctg 390
 Pro Glu Gly Ser Gly Leu Arg Ile Gln Asp Asn Asn Asn Leu Phe Leu
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 Ser Leu Gly Leu Gln Glu Lys Ile Leu Lys Lys Leu Lys Thr Val Glu
 120 125 130

 aac aaa atg aag aac cta gaa ggg ata atc gtt gct caa aaa cct gcc 486
 Asn Lys Met Lys Asn Leu Glu Gly Ile Ile Val Ala Gln Lys Pro Ala
 135 140 145

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 Thr Lys Arg Asp Cys Ser Ser Glu Pro Tyr Cys Ser Cys Ser Asp Cys
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 cag agt ccc ttg tcc aca tca ggg ttt act tcc ccc att tga aat gta 582
 Gln Ser Pro Leu Ser Thr Ser Gly Phe Thr Ser Pro Ile Asn Val
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 Val Ile Thr Leu Tyr Lys Leu Tyr Lys Lys Gly Ser His Ile Phe Glu
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160 200 PCT FINAL.ST25
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Leu Lys Thr Val Glu Asn Lys Met Lys Asn Leu Glu Gly Ile Ile Val
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Pro Ile

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Met Cys Phe Ala Gly Phe Ser Phe Lys Glu Lys Ile Phe Ile Ala Leu
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Gly Ala Leu Leu Met Gly Ile Leu Gly Pro Lys Met Leu Thr Arg His
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Tyr Asp Pro Ser Lys Ile Lys Leu Gln Leu Ser Thr Leu Glu His His
85 90 95

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agaattttaa agtagaaata tgtaggact gtacagaaaa tccaggattt agtaaacatg 469

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16U 200 PCT FINAL ST25

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Leu Glu Thr Ala Arg Val Ser Ala Pro His Leu Glu Pro Tyr Ala Lys
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Asp Val Met Ser Val Ala Phe Leu Ala Ile Ser Ile Thr Ala Pro Asn
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| Val Ser Arg Gly Val Glu Pro Leu Glu Ala Ala Arg Ala Gln Pro Ala | | | |
| 15 20 25 30 | | | |

aag gac agg agg gcc aag gga acc ccg aag tcc tcg aag ccc ggg aaa
 Lys Asp Arg Arg Ala Lys Gly Thr Pro Lys Ser Ser Lys Pro Gly Lys
 25 40 45

aaa cac cg^g tat ctg aga cta ctt cca gag g^cc ttg ata agg ttc gg^c 313
Lys His Arg Tyr Leu Arg Leu Leu Pro Glu Ala Leu Ile Arg Phe Gly
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 80 85 90

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Val Ser Thr Cys Cys Glu Cys Cys Asn Asn Ile Arg Cys Phe Met Ile
95          100          105          110

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| 115 120 125 | |

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 130 135 140

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gag aag ttg gca ttg gaa aag agt tac gat att tca tct ggc ctg gta      601
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16U 200 PCT FINAL.ST25
160 165 170

| | |
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| cca tcc att aat gaa gaa aat aaa caa agt aag gta gga att gaa gat Pro Ser Ile Asn Glu Glu Asn Lys Gln Ser Lys Val Gly Ile Glu Asp 195 200 205 | 745 |
| att tgc gaa gaa ata aag gtt gtc agt ggt tgc cag agc agt ggt ata Ile Cys Glu Glu Ile Lys Val Val Ser Gly Cys Gln Ser Ser Gly Ile 210 215 220 | 793 |
| tca ttc caa tca aaa tac ctg tct ttc atc ctt ggg cag act gtg Ser Phe Gln Ser Lys Tyr Leu Ser Phe Phe Ile leu Gly Gln Thr Val 225 230 235 | 841 |
| cag gga ata gca gga atg cct ctt tat atc ctt gga ata acc ttt att Gln Gly Ile Ala Gly Met Pro Leu Tyr Ile Leu Gly Ile Thr Phe Ile 240 245 250 | 889 |
| gat gag aat gtt gct aca cac tca gct ggt atc tat tta ggt att gca Asp Glu Asn Val Ala Thr His Ser Ala Gly Ile Tyr Leu Gly Ile Ala 255 260 265 270 | 937 |
| gaa tgt aca tca atg att gga tat gct ctg ggt tat gtg cta gga gca Glu Cys Thr Ser Met Ile Gly Tyr Ala Leu Gly Tyr Val Leu Gly Ala 275 280 285 | 985 |
| cca cta gtt aaa gtc cct gag aat act act tct gca aca aac act aca Pro Leu Val Lys Val Pro Glu Asn Thr Thr Ser Ala Thr Asn Thr Thr 290 295 300 | 1033 |
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| ctt ttt gcc gct gtc gtt gca tgg tgt acat tta ata cca ttg tca tgc Leu Phe Ala Ala Val Val Ala Trp Cys Thr Leu Ile Pro Leu Ser Cys 320 325 330 | 1129 |
| ttt cca aac aat atg cca ggt tca aca cgg ata aaa gct agg aaa cgt Phe Pro Asn Asn Met Pro Gly Ser Thr Arg Ile Lys Ala Arg Lys Arg 335 340 345 350 | 1177 |
| aaa cag ctt cat ttt ttt gac agc aga ctt aaa gat ctg aaa ctt gga Lys Gln Leu His Phe Phe Asp Ser Arg Leu Lys Asp Leu Lys Leu Gly 355 360 365 | 1225 |
| act aat atc aag gat tta tgt gct gct ctt tgg att ctg atg agg aat Thr Asn Ile Lys Asp Leu Cys Ala Ala Leu Trp Ile Leu Met Arg Asn 370 375 380 | 1273 |
| cca gtg ctc ata tgc cta gct ctg tca aaa gct aca gaa tat tta gtt Pro Val Leu Ile Cys Leu Ala Leu Ser Lys Ala Thr Glu Tyr Leu Val 385 390 395 | 1321 |
| att att gga gct tct gaa ttt ttg cct ata tat tta gaa aat cag ttt Ile Ile Gly Ala Ser Glu Phe Leu Pro Ile Tyr Leu Glu Asn Gln Phe 400 405 410 | 1369 |
| ata tta aca ccc act gtg gca act aca ctt gca gga ctt gtt tta att Ile Leu Thr Pro Thr Val Ala Thr Thr Leu Ala Gly Leu Val Leu Ile 415 420 425 430 | 1417 |
| cca gga ggt gca ctt ggc cag ctt ctg gga ggt gtc att gtt tcc aca Pro Gly Gly Ala Leu Gly Gln Leu Leu Gly Gly Val Ile Val Ser Thr 435 440 445 | 1465 |
| tta gaa atg tct tgt aaa gcc ctt atg aga ttt ata atg gtt aca tct Leu Glu Met Ser Cys Lys Ala Leu Met Arg Phe Ile Met Val Thr Ser 450 455 460 | 1513 |
| gtg ata tca ctt ata ctg ctt gtg ttt att att ttt gta cgc tgt aat Val Ile Ser Leu Ile Leu Leu Val Phe Ile Ile Phe Val Arg Cys Asn 465 470 475 | 1561 |
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| | | | |
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| Pro Val Gln Phe Ala Gly Ile Asn Glu Asp Tyr Asp Gly Thr Arg Lys | | | |
| 480 | 485 | 490 | |
| ttg gga aac ctc acg gct cct tgc aat gaa aaa tgt aga tgc tca tct | | | 1657 |
| Leu Gly Asn Leu Thr Ala Pro Cys Asn Glu Lys Cys Arg Cys Ser Ser | | | |
| 495 | 500 | 505 | 510 |
| tca att tat tct tct ata tgt gga aga gat gat att gaa tat ttt tct | | | 1705 |
| Ser Ile Tyr Ser Ser Ile Cys Gly Arg Asp Asp Ile Glu Tyr Phe Ser | | | |
| 515 | 520 | 525 | |
| gcc tgc ttt gca ggg tgt aca tat tct aaa gca caa aac caa aaa aag | | | 1753 |
| Ala Cys Phe Ala Gly Cys Thr Tyr Ser Lys Ala Gln Asn Gln Lys Lys | | | |
| 530 | 535 | 540 | |
| atg tac tac aat tgt tct tgc att aaa gaa gga tta ata act gca gat | | | 1801 |
| Met Tyr Tyr Asn Cys Ser Cys Ile Lys Glu Gly Leu Ile Thr Ala Asp | | | |
| 545 | 550 | 555 | |
| gca gaa ggt gat ttt att gat gcc aga ccc ggg aaa tgt gat gca aag | | | 1849 |
| Ala Glu Gly Asp Phe Ile Asp Ala Arg Pro Gly Lys Cys Asp Ala Lys | | | |
| 560 | 565 | 570 | |
| tgc tat aag tta cct ttg ttc att gct ttt atc ttt tct aca ctt ata | | | 1897 |
| Cys Tyr Lys Leu Pro Leu Phe Ile Ala Phe Ile Phe Ser Thr Leu Ile | | | |
| 575 | 580 | 585 | 590 |
| ttt tct ggt ttt tct ggt gta cca atc gtc ttg gcc atg acg cggt gtt | | | 1945 |
| Phe Ser Gly Phe Ser Gly Val Pro Ile Val Leu Ala Met Thr Arg Val | | | |
| 595 | 600 | 605 | |
| gta cct gac aaa ctg cgt tct ctg gcc ttg ggt gta agc tat gtg att | | | 1993 |
| Val Pro Asp Lys Leu Arg Ser Leu Ala Leu Gly Val Ser Tyr Val Ile | | | |
| 610 | 615 | 620 | |
| ttg aga ata ttt ggg act att cct gga cca tca atc ttt aaa atg tca | | | 2041 |
| Leu Arg Ile Phe Gly Thr Ile Pro Gly Pro Ser Ile Phe Lys Met Ser | | | |
| 625 | 630 | 635 | |
| gga gaa act tct tgt att tta cgg gat gtt aat aaa tgt gga cac aca | | | 2089 |
| Gly Glu Thr Ser Cys Ile Leu Arg Asp Val Asn Lys Cys Gly His Thr | | | |
| 640 | 645 | 650 | |
| gga cgt tgt tgg ata tat aac aag aca aaa atg gct ttc tta ttg gta | | | 2137 |
| Gly Arg Cys Trp Ile Tyr Asn Lys Thr Lys Met Ala Phe Leu Leu Val | | | |
| 655 | 660 | 665 | 670 |
| gga ata tgt ttt ctt tgc aaa cta tgc act atc atc ttc act act att | | | 2185 |
| Gly Ile Cys Phe Leu Cys Lys Leu Cys Thr Ile Ile Phe Thr Thr Ile | | | |
| 675 | 680 | 685 | |
| gca ttt ttc ata tac aaa cgt cgt cta aat gag aac act gac ttc cca | | | 2233 |
| Ala Phe Phe Ile Tyr Lys Arg Arg Leu Asn Glu Asn Thr Asp Phe Pro | | | |
| 690 | 695 | 700 | |
| gat gta act gtg aag aat cca aaa gtt aag aaa aaa gaa gaa act gac | | | 2281 |
| Asp Val Thr Val Lys Asn Pro Lys Val Lys Lys Glu Glu Thr Asp | | | |
| 705 | 710 | 715 | |
| ttg taactggatc atcattgtga ttgcagatca tttgaggatc agagtgtgaa | | | 2334 |
| <u>Leu</u> | | | |
| aacgagtttc tctttacag attctccaag atttgttct gtgcccaact ttcagaagag | | | 2394 |
| aaaaatcaca cattatgttt acataagtag caaaaatata ttatggtga tctgcatttt | | | 2454 |
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Thr Cys Cys Glu Cys Cys Asn Asn Ile Arg Cys Phe Met Ile Phe Tyr
100 105 110

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16U 200 PCT FINAL.ST25
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370 375 380

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Asn Leu Thr Ala Pro Cys Asn Glu Lys Cys Arg Cys Ser Ser Ser Ile
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565 570 575

Lys Leu Pro Leu Phe Ile Ala Phe Ile Phe Ser Thr Leu Ile Phe Ser
580 585 590

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Cys Phe Leu Cys Lys Leu Cys Thr Ile Ile Phe Thr Thr Ile Ala Phe
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10 15 20

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Val Leu Leu Val Gln Asn Arg Asp His Leu Tyr Asn Phe Leu Leu
25 30 35

aag atc aac ctc ttc aac cac tgg gtg tca ggg ctg gcc cag gag gcc 198
Lys Ile Asn Leu Phe Asn His Trp Val Ser Gly Leu Ala Gln Glu Ala
40 45 50

cgg ggg tcc tgt aac tgg cag gcc cac cta ccc ctg gga gct gca gcc 246
Arg Gly Ser Cys Asn Trp Gln Ala His Leu Pro Leu Gly Ala Ala Ala
55 60 65 70

tgc ccc ctg ggc cag gct ctc tgg gct ggg ctg gct ctg ata cag gtc 294
Cys Pro Leu Gly Gln Ala Leu Trp Ala Gly Leu Ala Leu Ile Gln Val
75 80 85

ccc gta tgg ctg gtg cta cag gga ccc agg ctg atg tgg gct ggc atg 342
Pro Val Trp Leu Val Leu Gln Gly Pro Arg Leu Met Trp Ala Gly Met
90 95 100

tgg ggc agc acc aag ggc ctg ggc ctg gct ctc agt gcc tgg gag 390
-Trp Gly Ser Thr Lys Gly Leu Gly Leu Ala Leu Ser Ala Trp Glu
105 110 115

cag ctg ggc ctg tct gtg gcc atc tgg aca gat ctg ttt ttg tca tgt 438
Gln Leu Gly Leu Ser Val Ala Ile Trp Thr Asp Leu Phe Leu Ser Cys
120 125 130

ctg cac ggc ctg atg ttg gtg gcc ttg ctc ttg gtg gta gtg acc tgg 486
Leu His Gly Leu Met Leu Val Ala Leu Leu Val Val Val Thr Trp
135 140 145 150

agg gtg tgt cag aag tcc cac tgc ttc cga ctg ggc agg cag ctc agt 534
Arg Val Cys Gln Lys Ser His Cys Phe Arg Leu Gly Arg Gln Leu Ser
155 160 165

aag gcc ttg caa gtg aac tgc gtg gta agg aag ctc ctg gta cag ctg 582
Lys Ala Leu Gln Val Asn Cys Val Val Arg Lys Leu Leu Val Gln Leu
170 175 180

16U 200 PCT FINAL.ST25
 aga cgt ctg tat tgg tgg gtg gag act atg act gcc ctc acc tcc tgg 630
 Arg Arg Leu Tyr Trp Trp Val Glu Thr Met Thr Ala Leu Thr Ser Trp
 185 190 195

cac ctg gcc tat ctc atc acc tgg acc acc tgc ctg gcc tcc cac ctg 678
 His Leu Ala Tyr Leu Ile Thr Trp Thr Cys Leu Ala Ser His Leu
 200 205 210

ctg cag gct gcc ttt gag cac acg acc cag ctg gcc gag gcc cag gag 726
 Leu Gln Ala Ala Phe Glu His Thr Thr Gln Leu Ala Glu Ala Gln Glu
 215 220 225 230

gtt gaa ccc cag gag gtc tca ggg tct tcc ttg ctg ccc tca ctg tct 774
 Val Glu Pro Gln Glu Val Ser Gly Ser Ser Leu Leu Pro Ser Leu Ser
 235 240 245

gcg tcc tcg gac tca gag tct gga aca gtt ttg cca gag caa gaa act 822
 Ala Ser Ser Asp Ser Glu Ser Gly Thr Val Leu Pro Glu Gln Glu Thr
 250 255 260

ccc aga gaa taaatgtatc cccatctgcc 851
 Pro Arg Glu
 265

<210> 249

<211> 265

<212> PRT

<213> Homo sapiens

<400> 249

Met Glu Ala Leu Pro Pro Val Arg Ser Ser Leu Leu Gly Ile Leu Leu
 1 5 10 15

Gln Val Thr Arg Leu Ser Val Leu Val Gln Asn Arg Asp His Leu
 20 25 30

Tyr Asn Phe Leu Leu Lys Ile Asn Leu Phe Asn His Trp Val Ser
 35 40 45

Gly Leu Ala Gln Glu Ala Arg Gly Ser Cys Asn Trp Gln Ala His Leu
 50 55 60

Pro Leu Gly Ala Ala Ala Cys Pro Leu Gly Gln Ala Leu Trp Ala Gly
 65 70 75 80

Leu Ala Leu Ile Gln Val Pro Val Trp Leu Val Leu Gln Gly Pro Arg
 85 90 95

Leu Met Trp Ala Gly Met Trp Gly Ser Thr Lys Gly Leu Gly Leu Ala
 100 105 110

Leu Leu Ser Ala Trp Glu Gln Leu Gly Leu Ser Val Ala Ile Trp Thr
 115 120 125

Asp Leu Phe Leu Ser Cys Leu His Gly Leu Met Leu Val Ala Leu Leu
 130 135 140

Leu Val Val Val Thr Trp Arg Val Cys Gln Lys Ser His Cys Phe Arg
 145 150 155 160

Leu Gly Arg Gln Leu Ser Lys Ala Leu Gln Val Asn Cys Val Val Arg
 165 170 175

Lys Leu Leu Val Gln Leu Arg Arg Leu Tyr Trp Trp Val Glu Thr Met
 180 185 190

160 200 PCT FINAL.ST25

Thr Ala Leu Thr Ser Trp His Leu Ala Tyr Leu Ile Thr Trp Thr Thr
 195 200 205

Cys Leu Ala Ser His Leu Leu Gln Ala Ala Phe Glu His Thr Thr Gln
 210 215 220

Leu Ala Glu Ala Gln Glu Val Glu Pro Gln Glu Val Ser Gly Ser Ser
 225 230 235 240

Leu Leu Pro Ser Leu Ser Ala Ser Ser Asp Ser Glu Ser Gly Thr Val
 245 250 255

Leu Pro Glu Gln Glu Thr Pro Arg Glu
 260 265

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aaagttcaga cccaggaaaa ttccatagt acctta atg aaa aag ata gaa atc 114
 Met Lys Lys Ile Glu Ile
 1 5

agt ggg acg tgt ctt tcc ttt cat ctc ctt ttc ggc ttg gaa atc aga 162
 Ser Gly Thr Cys Leu Ser Phe His Leu Leu Phe Gly Leu Glu Ile Arg
 10 15 20

atg aga agg att gtt ttt gct ggt gtt atc tta ttc cgc ctc tta ggt 210
 Met Arg Arg Ile Val Phe Ala Gly Val Ile Leu Phe Arg Leu Leu Gly
 25 30 35

gtt atc tta ttc cgc ctc tta ggt gtt atc tta ttc ggc cgc tta ggt 258
 Val Ile Leu Phe Arg Leu Leu Gly Val Ile Leu Phe Gly Arg Leu Gly
 40 45 50

gac ctg gga acc tgc cag aca aaa cct ggt cag tac tgg aaa gaa gag 306
 Asp Leu Gly Thr Cys Gln Thr Lys Pro Gly Gln Tyr Trp Lys Glu Glu
 55 60 65 70

gtc cac att caa gat gtt gga ggt ttg att tgc aag gca tgc aat ctt 354
 Val His Ile Gln Asp Val Gly Leu Ile Cys Arg Ala Cys Asn Leu
 75 80 85

tca ctg ccc ttc cat gga tgt ctt tta gac ctg gga acc tgc cag gca 402
 Ser Leu Pro Phe His Gly Cys Leu Leu Asp Leu Gly Thr Cys Gln Ala
 90 95 100

gaa cct ggt cag tac tgt aaa gaa gag gtc cac att caa ggt ggc att 450
 Glu Pro Gly Gln Tyr Cys Lys Glu Val His Ile Gln Gly Gly Ile
 105 110 115

caa tgg tat tca gtc aaa ggc tgc aca aag aac aca tca gag tgc ttc 498
 Gln Trp Tyr Ser Val Lys Gly Cys Thr Lys Asn Thr Ser Glu Cys Phe
 120 125 130

aag agt act ctc gtc aag aga att ctg caa ctg cat gaa ctt gta act 546
 Lys Ser Thr Leu Val Lys Arg Ile Leu Gln Leu His Glu Leu Val Thr
 135 140 145 150

act cac tgc tgc aat cat tct ttg tgc aat ttc tgatgcgtg gccccatatct 599
 Thr His Cys Cys Asn His Ser Leu Cys Asn Phe
 155 160

aaaatgcctg gcagatcaat cagtcgtcgtt gctatcacaa aatgatggct 659

160 200 PCT FINAL.ST25

attgtcaatt agcccacttc agaaaacctca gacccttgcg ggtagaagga attttgatct 719
 gaaattgact ttgggtttca atattcccaa tatctcccc accacccca actcatctga 779
 gaaat 784

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 <212> PRT
 <213> Homo sapiens

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Phe Gly Leu Glu Ile Arg Met Arg Arg Ile Val Phe Ala Gly Val Ile
 20 25 30

Leu Phe Arg Leu Leu Gly Val Ile Leu Phe Arg Leu Leu Gly Val Ile
 35 40 45

Leu Phe Gly Arg Leu Gly Asp Leu Gly Thr Cys Gln Thr Lys Pro Gly
 50 55 60

Gln Tyr Trp Lys Glu Glu Val His Ile Gln Asp Val Gly Gly Leu Ile
 65 70 75 80

Cys Arg Ala Cys Asn Leu Ser Leu Pro Phe His Gly Cys Leu Leu Asp
 85 90 95

Leu Gly Thr Cys Gln Ala Glu Pro Gly Gln Tyr Cys Lys Glu Glu Val
 100 105 110

His Ile Gln Gly Gly Ile Gln Trp Tyr Ser Val Lys Gly Cys Thr Lys
 115 120 125

Asn Thr Ser Glu Cys Phe Lys Ser Thr Leu Val Lys Arg Ile Leu Gln
 130 135 140

Leu His Glu Leu Val Thr Thr His Cys Cys Asn His Ser Leu Cys Asn
 145 150 155 160

Phe

<210> 252
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 Met Ala Glu Ala Ser Arg Trp His Arg Gly
 1 5 10

ggg gct tcg aaa cat aag ttg cat tac aga aag gaa gta gaa att aca 101
 Gly Ala Ser Lys His Lys Leu His Tyr Arg Lys Glu Val Glu Ile Thr
 15 20 25

acc aca ctt cag gaa ttg tta ctc tac ttt att ttt tta ata aac cta 149

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| | | | |
|--|-----|-----|------|
| Thr Thr Leu Gln Glu Leu Leu Leu Tyr Phe Ile Phe Leu Ile Asn Leu | | | |
| 30 | 35 | 40 | |
| tgt ata ttg act ttt ggg atg gta aac cca cat atg tat tac tta aac | | | 197 |
| Cys Ile Leu Thr Phe Gly Met Val Asn Pro His Met Tyr Tyr Leu Asn | | | |
| 45 | 50 | 55 | |
| aag gtt atg tca tct cta ttt ttg gac act tct gtg cct ggt gaa gaa | | | 245 |
| Lys Val Met Ser Ser Leu Phe Leu Asp Thr Ser Val Pro Gly Glu Glu | | | |
| 60 | 65 | 70 | |
| aga acc aac ttt aag tcc att cgc agc ata act gat ttt tgg aag ttt | | | 293 |
| Arg Thr Asn Phe Lys Ser Ile Arg Ser Ile Thr Asp Phe Trp Lys Phe | | | |
| 75 | 80 | 85 | 90 |
| atg gaa gga ccc ctt ttg gaa ggt ctg tac tgg gat tca tgg tac aat | | | 341 |
| Met Glu Gly Pro Leu Leu Glu Gly Leu Tyr Trp Asp Ser Trp Tyr Asn | | | |
| 95 | 100 | 105 | |
| aac cag cag ctg tat aat tta aag aac agc agt cgc atc tac tat gaa | | | 389 |
| Asn Gln Gln Leu Tyr Asn Leu Lys Asn Ser Ser Arg Ile Tyr Tyr Glu | | | |
| 110 | 115 | 120 | |
| aat ata ctt cta gga gtt ccc aga gtt cgt caa cta aaa gtc cgc aac | | | 437 |
| Asn Ile Leu Leu Gly Val Pro Arg Val Arg Gln Leu Lys Val Arg Asn | | | |
| 125 | 130 | 135 | |
| aac aca tgc aaa gtc tat tca tct ttt cag tct ttg atg agt gaa tgt | | | 485 |
| Asn Thr Cys Lys Val Tyr Ser Ser Phe Gln Ser Leu Met Ser Glu Cys | | | |
| 140 | 145 | 150 | |
| tat ggc aaa tat act tct gca aat gaa gac ctc tct aat ttt ggc ctt | | | 533 |
| Tyr Gly Lys Tyr Thr Ser Ala Asn Glu Asp Leu Ser Asn Phe Gly Leu | | | |
| 155 | 160 | 165 | 170 |
| caa att aat act gaa tgg aga tat tct act tct aat acc aac tcc cct | | | 581 |
| Gln Ile Asn Thr Glu Trp Arg Tyr Ser Thr Ser Asn Thr Asn Ser Pro | | | |
| 175 | 180 | 185 | |
| tgg cac tgg gga ttt ctt ggt gtt tac cga aat ggg gga tac att ttc | | | 629 |
| Trp His Trp Phe Leu Gly Val Tyr Arg Asn Gly Gly Tyr Ile Phe | | | |
| 190 | 195 | 200 | |
| act tta tca aaa tcg aaa tct gaa acc aaa aac aag ttc att gac ctt | | | 677 |
| Thr Leu Ser Lys Ser Lys Ser Glu Thr Lys Asn Lys Phe Ile Asp Leu | | | |
| 205 | 210 | 215 | |
| cga ctg aac agc tgg atc aca aga ggg act aga gtt att ttt att gat | | | 725 |
| Arg Leu Asn Ser Trp Ile Thr Arg Gly Thr Arg Val Ile Phe Ile Asp | | | |
| 220 | 225 | 230 | |
| ttt tcc tta tat aat gct aat gta aat cta ttt tgt att atc aga ttg | | | 773 |
| Phe Ser Leu Tyr Asn Ala Asn Val Asn Leu Phe Cys Ile Ile Arg Leu | | | |
| 235 | 240 | 245 | 250 |
| gtg gca gaa ttc cct gca act gga gga ata ctt act tca tgg cag ttt | | | 821 |
| Val Ala Glu Phe Pro Ala Thr Gly Gly Ile Leu Thr Ser Trp Gln Phe | | | |
| 255 | 260 | 265 | |
| tac tct gtg aag ctc ctc aga tat gtt agc tac tat gac tat ttt att | | | 869 |
| -Tyr Ser Val Lys Leu Leu Arg Tyr Val Ser Tyr Tyr Asp Tyr Phe Ile | | | |
| 270 | 275 | 280 | |
| gct tcc tgt gaa atc aca ttc tgt att ttt ctt ttt gtc ttc aca aca | | | 917 |
| Ala Ser Cys Glu Ile Thr Phe Cys Ile Phe Leu Phe Val Phe Thr Thr | | | |
| 285 | 290 | 295 | |
| caa gaa gtc aaa aaa ata aaa gaa ttt aag tct gcc tat ttc aaa agt | | | 965 |
| Gln Glu Val Lys Lys Ile Lys Glu Phe Lys Ser Ala Tyr Phe Lys Ser | | | |
| 300 | 305 | 310 | |
| att tgg aac tgg cta gaa ttg cta ctt ttg ctg ttg tgg ttt gtg gct | | | 1013 |
| Ile Trp Asn Trp Leu Glu Leu Leu Leu Leu Cys Phe Val Ala | | | |
| 315 | 320 | 325 | 330 |
| gtt tcc ttc aac aca tac tat aat gta caa att ttt ctc tta ctt gga | | | 1061 |
| Val Ser Phe Asn Thr Tyr Tyr Asn Val Gln Ile Phe Leu Leu Leu Gly | | | |
| 335 | 340 | 345 | |

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| | |
|---|------|
| cag ctg ttg aaa agt act gaa aaa tat tca gat ttc tat ttt ctt gca Gln Leu Leu Lys Ser Thr Glu Lys Tyr Ser Asp Phe Tyr Phe Leu Ala 350 355 360 | 1109 |
| tgc tgg cac att tat tac aat aat ata att gct att acc atc ttt ttt Cys Trp His Ile Tyr Tyr Asn Asn Ile Ile Ala Ile Thr Ile Phe Phe 365 370 375 | 1157 |
| gca tgg ata aag ata ttc aaa ttc ata agc ttt aac aag aca atg tct Ala Trp Ile Lys Ile Phe Lys Phe Ile Ser Phe Asn Lys Thr Met Ser 380 385 390 | 1205 |
| cag ctg tca tca acc ttg tcc cgt tgt gtt aaa gac ata gta gga ttt Gln Leu Ser Ser Thr Leu Ser Arg Cys Val Lys Asp Ile Val Gly Phe 395 400 405 410 | 1253 |
| gcc atc atg ttt ttt ata ata ttc ttt gct tat gcc cag tta gga ttt Ala Ile Met Phe Phe Ile Ile Phe Phe Ala Tyr Ala Gln Leu Gly Phe 415 420 425 | 1301 |
| ctt gtt ttt gga tca caa gtt gat gac ttt tcc act ttt cag aat tcc Leu Val Phe Gly Ser Gln Val Asp Asp Phe Ser Thr Phe Gln Asn Ser 430 435 440 | 1349 |
| ata ttt gca caa ttt cga att gtt ctt gga gat ttt aat ttt gct ggt Ile Phe Ala Gln Phe Arg Ile Val Leu Gly Asp Phe Asn Phe Ala Gly 445 450 455 | 1397 |
| att cag caa gcc aat cct atc ttg gga ccc att tac ttc atc act ttc Ile Gln Gln Ala Asn Pro Ile Leu Gly Pro Ile Tyr Phe Ile Thr Phe 460 465 470 | 1445 |
| atc ttt ttt gtg ttc ttt gtc ctg ctg aat atg ttc ttg gca att att Ile Phe Phe Val Phe Val Leu Leu Asn Met Phe Leu Ala Ile Ile 475 480 485 490 | 1493 |
| aat gat acc tat tct gaa gtg aaa gct gac tat tca ata ggc aga agg Asn Asp Thr Tyr Ser Glu Val Lys Ala Asp Tyr Ser Ile Gly Arg Arg 495 500 505 | 1541 |
| cca gat ttt gaa ctt ggc aaa atg att aaa cag agt tac aaa aat gtt Pro Asp Phe Glu Leu Gly Lys Met Ile Lys Gln Ser Tyr Lys Asn Val 510 515 520 | 1589 |
| ctc gag aaa ttc aga ctg aag aaa gct caa aaa gat gaa gac aag aaa Leu Glu Lys Phe Arg Leu Lys Ala Gln Lys Asp Glu Asp Lys Lys 525 530 535 | 1637 |
| acc aaa ggc agc gga gat ttg gct gaa caa gcc aga aga gaa ggc ttt Thr Lys Gly Ser Gly Asp Leu Ala Glu Gln Ala Arg Arg Glu Gly Phe 540 545 550 | 1685 |
| gac gaa aat gag att caa aac gca gag cag atg aaa aaa tgg aaa gag Asp Glu Asn Glu Ile Gln Asn Ala Glu Gln Met Lys Lys Trp Lys Glu 555 560 565 570 | 1733 |
| agg ctt gag aaa aag tat tat tct atg gaa att caa gat gac tac cag Arg Leu Glu Lys Tyr Tyr Ser Met Glu Ile Gln Asp Asp Tyr Gln 575 580 585 | 1781 |
| -cct gtc act caa gaa gaa ttt cga gat ggc acc aca acc aac tac aaa Pro Val Thr Gln Glu Glu Phe Arg Asp Gly Thr Thr Lys Tyr Lys 590 595 600 | 1829 |
| atg aga ttc tct ctg agt gcc tgacaaaaacg aatattaagta ccagccaagt Met Arg Phe Ser Leu Ser Ala 605 | 1880 |
| acacacgtg atagttcaa ggaatacaac tgactttatg atatgaattt tcaaggaaacg | 1940 |
| tatcttatat ggatttgaa gaatcttgtt tgcttataag aacctcaaga agcctaagct | 2000 |
| tggcttaat tttcttgtac tctctgtact cctcaagcac tggAACACGA tcctttct | 2060 |
| gggcattcct agggagaaa ataaaaatttg taatgttcta gagatcattt ggaaaaaaag | 2120 |
| atccaaaagt tgtcttaata tgagacatac tgttactaaa cataagttca aataaaaaagt | 2180 |
| tgttctgaaa aaaaaaaaaa aaaaa | 2205 |

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<210> 253
<211> 609
<212> PRT
<213> Homo sapiens

<400> 253

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Leu Leu Tyr Phe Ile Phe Leu Ile Asn Leu Cys Ile Leu Thr Phe Gly
35 40 45

Met Val Asn Pro His Met Tyr Tyr Leu Asn Lys Val Met Ser Ser Leu
50 55 60

Phe Leu Asp Thr Ser Val Pro Gly Glu Glu Arg Thr Asn Phe Lys Ser
65 70 75 80

Ile Arg Ser Ile Thr Asp Phe Trp Lys Phe Met Glu Gly Pro Leu Leu
85 90 95

Glu Gly Leu Tyr Trp Asp Ser Trp Tyr Asn Asn Gln Gln Leu Tyr Asn
100 105 110

Leu Lys Asn Ser Ser Arg Ile Tyr Tyr Glu Asn Ile Leu Leu Gly Val
115 120 125

Pro Arg Val Arg Gln Leu Lys Val Arg Asn Asn Thr Cys Lys Val Tyr
130 135 140

Ser Ser Phe Gln Ser Leu Met Ser Glu Cys Tyr Gly Lys Tyr Thr Ser
145 150 155 160

Ala Asn Glu Asp Leu Ser Asn Phe Gly Leu Gln Ile Asn Thr Glu Trp
165 170 175

Arg Tyr Ser Thr Ser Asn Thr Asn Ser Pro Trp His Trp Gly Phe Leu
180 185 190

Gly Val Tyr Arg Asn Gly Gly Tyr Ile Phe Thr Leu Ser Lys Ser Lys
195 200 205

Ser Glu Thr Lys Asn Lys Phe Ile Asp Leu Arg Leu Asn Ser Trp Ile
210 215 220

Thr Arg Gly Thr Arg Val Ile Phe Ile Asp Phe Ser Leu Tyr Asn Ala
225 230 235 240

Asn Val Asn Leu Phe Cys Ile Ile Arg Leu Val Ala Glu Phe Pro Ala
245 250 255

Thr Gly Gly Ile Leu Thr Ser Trp Gln Phe Tyr Ser Val Lys Leu Leu
260 265 270

Arg Tyr Val Ser Tyr Tyr Asp Tyr Phe Ile Ala Ser Cys Glu Ile Thr
275 280 285

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Phe Cys Ile Phe Leu Phe Val Phe Thr Thr Gln Glu Val Lys Lys Ile
290 295 300

Lys Glu Phe Lys Ser Ala Tyr Phe Lys Ser Ile Trp Asn Trp Leu Glu
305 310 315 320

Leu Leu Leu Leu Leu Cys Phe Val Ala Val Ser Phe Asn Thr Tyr
325 330 335

Tyr Asn Val Gln Ile Phe Leu Leu Leu Gly Gln Leu Leu Lys Ser Thr
340 345 350

Glu Lys Tyr Ser Asp Phe Tyr Phe Leu Ala Cys Trp His Ile Tyr Tyr
355 360 365

Asn Asn Ile Ile Ala Ile Thr Ile Phe Phe Ala Trp Ile Lys Ile Phe
370 375 380

Lys Phe Ile Ser Phe Asn Lys Thr Met Ser Gln Leu Ser Ser Thr Leu
385 390 395 400

Ser Arg Cys Val Lys Asp Ile Val Gly Phe Ala Ile Met Phe Phe Ile
405 410 415

Ile Phe Phe Ala Tyr Ala Gln Leu Gly Phe Leu Val Phe Gly Ser Gln
420 425 430

Val Asp Asp Phe Ser Thr Phe Gln Asn Ser Ile Phe Ala Gln Phe Arg
435 440 445

Ile Val Leu Gly Asp Phe Asn Phe Ala Gly Ile Gln Gln Ala Asn Pro
450 455 460

Ile Leu Gly Pro Ile Tyr Phe Ile Thr Phe Ile Phe Phe Val Phe Phe
465 470 475 480

Val Leu Leu Asn Met Phe Leu Ala Ile Ile Asn Asp Thr Tyr Ser Glu
485 490 495

Val Lys Ala Asp Tyr Ser Ile Gly Arg Arg Pro Asp Phe Glu Leu Gly
500 505 510

Lys Met Ile Lys Gln Ser Tyr Lys Asn Val Leu Glu Lys Phe Arg Leu
515 520 525

Lys Lys Ala Gln Lys Asp Glu Asp Lys Lys Thr Lys Gly Ser Gly Asp
530 535 540

Leu Ala Glu Gln Ala Arg Arg Glu Gly Phe Asp Glu Asn Glu Ile Gln
545 550 555 560

Asn Ala Glu Gln Met Lys Lys Trp Lys Glu Arg Leu Glu Lys Lys Tyr
565 570 575

Tyr Ser Met Glu Ile Gln Asp Asp Tyr Gln Pro Val Thr Gln Glu Glu
580 585 590

Phe Arg Asp Gly Thr Thr Lys Tyr Lys Met Arg Phe Ser Leu Ser

16U 200_PCT_FINAL.ST25
595 600 605

Ala

<210> 254
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<223>

<400> 254

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| atg | gcc | gct | tac | caa | caa | gaa | gag | cag | atg | cag | ctt | ccc | cga | gct | gat | | 48 |
| Met | Ala | Ala | Tyr | Gln | Gln | Glu | Glu | Gln | Met | Gln | Leu | Pro | Arg | Ala | Asp | | |
| 1 | | | | | | | | | 5 | 10 | | | | | 15 | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|----|
| gcc | att | cgt | tca | cgt | ctc | atc | gat | act | ttc | tct | ctc | att | gag | cat | ttg | | 96 |
| Ala | Ile | Arg | Ser | Arg | Leu | Ile | Asp | Thr | Phe | Ser | Leu | Ile | Glu | His | Leu | | |
| 20 | | | | | | | | | 25 | | | 30 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| caa | ggc | ttg | agc | caa | gct | gtg | ccg | cgg | cac | act | atc | agg | gag | tta | ctt | | 144 |
| Gln | Gly | Leu | Ser | Gln | Ala | Val | Pro | Arg | His | Thr | Ile | Arg | Glu | Leu | Leu | | |
| 35 | | | | | | | | | 40 | | | 45 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| gat | cct | tcc | cgc | cag | aag | aaa | ctt | gta | ttg | gga | gat | caa | cac | cag | cta | | 192 |
| Asp | Pro | Ser | Arg | Gln | Lys | Lys | Leu | Val | Leu | Gly | Asp | Gln | His | Gln | Leu | | |
| 50 | | | | | | | | | 55 | | | 60 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| gtg | cgt | ttc | tct | ata | aag | cct | cag | cgt | ata | gaa | cag | att | tca | cat | gcc | | 240 |
| Val | Arg | Phe | Ser | Ile | Lys | Pro | Gln | Arg | Ile | Glu | Gln | Ile | Ser | His | Ala | | |
| 65 | | | | | | | | | 70 | | | 75 | | 80 | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| cag | agg | ctg | ttg | agc | agg | ctt | cat | gtg | cgc | tgc | agt | cag | agg | cca | cct | | 288 |
| Gln | Arg | Leu | Leu | Ser | Arg | Leu | His | Val | Arg | Cys | Ser | Gln | Arg | Pro | Pro | | |
| 85 | | | | | | | | | 90 | | | 95 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| ctt | tct | ttg | tgg | gcc | gga | ttg | gtc | ctt | gag | tgt | cct | ctc | ttc | aaa | aac | | 336 |
| Leu | Ser | Leu | Trp | Ala | Gly | Trp | Val | Leu | Glu | Cys | Pro | Leu | Phe | Lys | Asn | | |
| 100 | | | | | | | | | 105 | | | 110 | | | | | |

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| ttc | atc | atc | tcc | ctg | ttt | ttg | aat | acg | atc | ata | ttg | atg | gtt | gaa | | 384 |
| Phe | Ile | Ile | Phe | Leu | Val | Phe | Leu | Asn | Thr | Ile | Ile | Leu | Met | Val | Glu | |
| 115 | | | | | | | | | 120 | | | 125 | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| ata | gaa | ttg | ctg | gaa | tcc | aca | aat | acc | aaa | cta | tgg | cca | ttg | aag | ctg | | 432 |
| Ile | Glu | Leu | Leu | Glu | Ser | Thr | Asn | Thr | Lys | Leu | Trp | Pro | Leu | Lys | Leu | | |
| 130 | | | | | | | | | 135 | | | 140 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| acc | ttg | gag | gtg | gca | gct | ttg | ttt | atc | ttg | ctt | att | ttc | atc | ctg | gag | | 480 |
| Thr | Leu | Glu | Val | Ala | Ala | Trp | Phe | Ile | Leu | Ile | Phe | Ile | Leu | Glu | | | |
| 145 | | | | | | | | | 150 | | | 155 | | 160 | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| atc | ctt | ctt | aag | tgg | cta | tcc | aac | ttt | tct | gtt | ttc | tgg | aag | agt | gcc | | 528 |
| Ile | Leu | Leu | Lys | Trp | Leu | Ser | Asn | Phe | Ser | Val | Phe | Trp | Lys | Ser | Ala | | |
| 165 | | | | | | | | | 170 | | | 175 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| tgg | aat | gtc | ttt | gac | ttt | gtt | acc | atg | ttg | tcc | ctg | ctt | ccc | gag | | 576 | |
| Trp | Asn | Val | Phe | Asp | Phe | Val | Val | Thr | Met | Leu | Ser | Leu | Leu | Pro | Glu | | |
| 180 | | | | | | | | | 185 | | | 190 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| gtt | gtg | gta | ttg | gta | ggg | gta | aca | ggc | caa | tgc | gtg | tgg | ctt | cag | ttt | | 624 |
| Val | Val | Val | Leu | Val | Gly | Val | Thr | Gly | Gln | Ser | Val | Trp | Leu | Gln | Leu | | |
| 195 | | | | | | | | | 200 | | | 205 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| ctg | agg | atc | tgc | cg | gtg | ctg | agg | tct | ctc | aaa | ctc | ctt | gca | caa | tcc | | 672 |
| Leu | Arg | Ile | Cys | Arg | Val | Leu | Arg | Ser | Leu | Lys | Leu | Leu | Ala | Gln | Phe | | |
| 210 | | | | | | | | | 215 | | | 220 | | | | | |

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| cgt | caa | att | caa | att | att | ttt | gtt | gtc | ctg | gtc | agg | gcc | ctc | aag | agc | | 720 |
| Arg | Gln | Ile | Gln | Ile | Ile | Leu | Val | Leu | Val | Arg | Ala | Leu | Lys | Ser | | | |
| 225 | | | | | | | | | 230 | | | 235 | | 240 | | | |

| | | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
| atg | acc | tcc | ctc | ttg | atg | ttt | gtt | ctg | ctc | atc | ttc | ttc | tac | att | ttt | gct | | 768 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|

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| | | | |
|---|-----|-----|------|
| Met Thr Phe Leu Leu Met Leu Leu Leu Ile Phe Phe Tyr Ile Phe Ala | | | |
| 245 | 250 | 255 | |
| gtg act ggt gtc tac gtc ttc tca gag tac acc cgt tca cct cgt cag | | | 816 |
| Val Thr Gly Val Tyr Val Phe Ser Glu Tyr Thr Arg Ser Pro Arg Gln | | | |
| 260 | 265 | 270 | |
| gac ctg gag tac cat gtg ttc ttc tcg gac ctc ccg aat tcc ctg gta | | | 864 |
| Asp Leu Glu Tyr His Val Phe Phe Ser Asp Leu Pro Asn Ser Leu Val | | | |
| 275 | 280 | 285 | |
| aca gtg ttc att ctc ttc acc ttg gat cat tgg tat gca ctg ctt cag | | | 912 |
| Thr Val Phe Ile Leu Phe Thr Leu Asp His Trp Tyr Ala Leu Leu Gln | | | |
| 290 | 295 | 300 | |
| gac gtc tgg aag gtg cct gaa gtc agt cgc atc ttc agc agc atc tat | | | 960 |
| Asp Val Trp Lys Val Pro Glu Val Ser Arg Ile Phe Ser Ser Ile Tyr | | | |
| 305 | 310 | 315 | 320 |
| ttc atc ctt tgg ttg ctt ggc tcc att atc ttt cga agt atc ata | | | 1008 |
| Phe Ile Leu Trp Leu Leu Leu Gly Ser Ile Ile Phe Arg Ser Ile Ile | | | |
| 325 | 330 | 335 | |
| gta gcc atg atg gtt act aac ttt cag aat atc agg aaa gag ctg aat | | | 1056 |
| Val Ala Met Met Val Thr Asn Phe Gln Asn Ile Arg Lys Glu Leu Asn | | | |
| 340 | 345 | 350 | |
| gag gag atg gcg cgt cgg gag gtt cag ctc aaa gct gac atg ttc aag | | | 1104 |
| Glu Glu Met Ala Arg Arg Glu Val Gln Leu Lys Ala Asp Met Phe Lys | | | |
| 355 | 360 | 365 | |
| cgg cag atc atc cag agg aga aaa aac atg tca cat gaa gca ctg acg | | | 1152 |
| Arg Gln Ile Ile Gln Arg Arg Lys Asn Met Ser His Glu Ala Leu Thr | | | |
| 370 | 375 | 380 | |
| tca agc cat agc aaa ata gag gac aga gga gct agt caa caa agg gaa | | | 1200 |
| Ser Ser His Ser Lys Ile Glu Asp Arg Gly Ala Ser Gln Gln Arg Glu | | | |
| 385 | 390 | 395 | 400 |
| agt ttg gac tta tca gaa gtg tct gaa gta gag tct aat tat ggt gcc | | | 1248 |
| Ser Leu Asp Leu Ser Glu Val Ser Glu Val Glu Ser Asn Tyr Gly Ala | | | |
| 405 | 410 | 415 | |
| act gaa gag gat tta ata aca tct gca tca aaa aca gaa gag acc ttg | | | 1296 |
| Thr Glu Glu Asp Leu Ile Thr Ser Ala Ser Lys Thr Glu Glu Thr Leu | | | |
| 420 | 425 | 430 | |
| tca aaa aag aga gag tac cag tct tcc tcc tgt gtc tcc tcc aca tcc | | | 1344 |
| Ser Lys Lys Arg Glu Tyr Gln Ser Ser Ser Cys Val Ser Ser Thr Ser | | | |
| 435 | 440 | 445 | |
| tct tcc tat tct tcc tct tct gaa tcc aga ttt tct gaa tct att ggt | | | 1392 |
| Ser Ser Tyr Ser Ser Ser Ser Glu Ser Arg Phe Ser Glu Ser Ile Gly | | | |
| 450 | 455 | 460 | |
| cgt ttg gac tgg gag act ctt gtg cac gaa aat ctg ccc ggg cta atg | | | 1440 |
| Arg Leu Asp Trp Glu Thr Leu Val His Glu Asn Leu Pro Gly Leu Met | | | |
| 465 | 470 | 475 | 480 |
| gaa atg gat cag gat gac cgt gtt tgg ccc aga gac tca ctc ttc cga | | | 1488 |
| Glu Met Asp Gln Asp Asp Arg Val Trp Pro Arg Asp Ser Leu Phe Arg | | | |
| 485 | 490 | 495 | |
| tat ttt gag ttg cta gaa aag ctt cag tat aac cta gag gaa cgt aag | | | 1536 |
| Tyr Phe Glu Leu Leu Lys Leu Gln Tyr Asn Leu Glu Glu Arg Lys | | | |
| 500 | 505 | 510 | |
| aag tta caa gag ttt gca gtg cag gca ctg atg aac ttg gaa gac aag | | | 1584 |
| Lys Leu Gln Glu Phe Ala Val Gln Ala Leu Met Asn Leu Glu Asp Lys | | | |
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<400> 255

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Gln Gly Leu Ser Gln Ala Val Pro Arg His Thr Ile Arg Glu Leu Leu
 35 40 45

Asp Pro Ser Arg Gln Lys Lys Leu Val Leu Gly Asp Gln His Gln Leu
 50 55 60

Val Arg Phe Ser Ile Lys Pro Gln Arg Ile Glu Gln Ile Ser His Ala
 65 70 75 80

Gln Arg Leu Leu Ser Arg Leu His Val Arg Cys Ser Gln Arg Pro Pro
 85 90 95

Leu Ser Leu Trp Ala Gly Trp Val Leu Glu Cys Pro Leu Phe Lys Asn
 100 105 110

Phe Ile Ile Phe Leu Val Phe Leu Asn Thr Ile Ile Leu Met Val Glu
 115 120 125

Ile Glu Leu Leu Glu Ser Thr Asn Thr Lys Leu Trp Pro Leu Lys Leu
 130 135 140

Thr Leu Glu Val Ala Ala Trp Phe Ile Leu Leu Ile Phe Ile Leu Glu
 145 150 155 160

Ile Leu Leu Lys Trp Leu Ser Asn Phe Ser Val Phe Trp Lys Ser Ala.
 165 170 175

Trp Asn Val Phe Asp Phe Val Val Thr Met Leu Ser Leu Leu Pro Glu
 180 185 190

Val Val Val Leu Val Gly Val Thr Gly Gln Ser Val Trp Leu Gln Leu
 195 200 205

Leu Arg Ile Cys Arg Val Leu Arg Ser Leu Lys Leu Leu Ala Gln Phe
 210 215 220

Arg Gln Ile Gln Ile Ile Leu Val Leu Val Arg Ala Leu Lys Ser
 225 230 235 240

Met Thr Phe Leu Leu Met Leu Leu Ile Phe Phe Tyr Ile Phe Ala
 245 250 255

Val Thr Gly Val Tyr Val Phe Ser Glu Tyr Thr Arg Ser Pro Arg Gln
 260 265 270

Asp Leu Glu Tyr His Val Phe Phe Ser Asp Leu Pro Asn Ser Leu Val
 275 280 285

Thr Val Phe Ile Leu Phe Thr Leu Asp His Trp Tyr Ala Leu Leu Gln
 290 295 300

Asp Val Trp Lys Val Pro Glu Val Ser Arg Ile Phe Ser Ser Ile Tyr

305 310 315 320 16U 200 PCT FINAL.ST25

Phe Ile Leu Trp Leu Leu Gly Ser Ile Ile Phe Arg Ser Ile Ile
 325 330 335

Val Ala Met Met Val Thr Asn Phe Gln Asn Ile Arg Lys Glu Leu Asn
340 345 350

Glu Glu Met Ala Arg Arg Glu Val Gln Leu Lys Ala Asp Met Phe Lys
355 360 365

Arg Gln Ile Ile Gln Arg Arg Lys Asn Met Ser His Glu Ala Leu Thr
370 375 380

Ser Ser His Ser Lys Ile Glu Asp Arg Gly Ala Ser Gln Gln Arg Glu
385 390 395 400

Ser Leu Asp Leu Ser Glu Val Ser Glu Val Glu Ser Asn Tyr Gly Ala
405 410 415

Thr Glu Glu Asp Leu Ile Thr Ser Ala Ser Lys Thr Glu Glu Thr Leu
420 425 430

Ser Lys Lys Arg Glu Tyr Gln Ser Ser Ser Cys Val Ser Ser Thr Ser
435 440 445

Ser Ser Tyr Ser Ser Ser Ser Glu Ser Arg Phe Ser Glu Ser Ile Gly
450 455 460

Arg Leu Asp Trp Glu Thr Leu Val His Glu Asn Leu Pro Gly Leu Met
465 470 475 480

Glu Met Asp Gln Asp Asp Arg Val Trp Pro Arg Asp Ser Leu Phe Arg
485 490 495

Tyr Phe Glu Leu Leu Glu Lys Leu Gin Tyr Asn Leu Glu Glu Arg Lys
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| <211> 50 | |
| <212> DNA | |
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| aatttcttat taaaagacc tcagaaatgt caccatgctt agttatTTTA | 50 |
| <210> 263 | |
| <211> 23 | |
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| ggccatggac aatgtcacag cag | 23 |
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| <400> 264 | |
| agcagacaca tactggccca ttccataacca c | 31 |
| <210> 265 | |
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| <400> 265 | |
| ggtactattc tatattttgg gcacacagca atgaagaaaa cagaaaaacc | 50 |
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16U 200 PCT FINAL.ST25

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